

**Cognitive Remediation Therapy for Young Female Adolescents with  
Anorexia Nervosa – Assessing the Feasibility of a Novel Eating Disorder  
Intervention**

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*It is the mark of an educated mind to be able to entertain a thought without accepting it*

Aristotle

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## ABBREVIATIONS

ADHD	Attention Deficit Hyperactivity Disorder
AN	Anorexia Nervosa
ANCOVA	Analysis of Covariance
BDI	Beck's Depression Inventory
BN	Bulimia Nervosa
BMI	Body Mass Index
BRI	Beck's Depression Inventory
BRIEF	Behavior Rating of Executive Function
CBT	Cognitive Behavioural Therapy
CCI	Central Coherence Index
CFS	Cognitive Flexibility Scale
ChOCI	Children's Obsessional Compulsive Inventory
CHQ	Child Health Questionnaire
CREST	Cognitive remediation and emotion skills training
CRT	Cognitive Remediation Therapy
CWIT	Color Word Interference Test
CY-BOCS	Children's Yale-Brown Obsessive Compulsive Scale
D-KEFS	Delis Kaplan Executive Functioning System
DOI	Duration of illness
DSM	Diagnostic and Statistical Manual of Mental Disorders
EAT-26	Eating Attitudes Test –26
EBW	Expected Body Weight
ED	Eating Disorder
EDBQ	Eating Disorders Belief Questionnaire
EDE	Eating Disorder Examination
EDE-Q	Eating Disorder Examination Questionnaire
EDI-2	Eating Disorder Inventory-2
EDNOS	Eating Disorder Not Otherwise Specified
FBT	Family Based Therapy
FMDPS	Frost's Multi-Dimensional Perfectionism Scale
GAF	Global Assessment of Functioning Scale
GEC	Global Executive Composite
GEFT	Group Embedded Figures Test
HADS	Hospital Anxiety and Depression Scale
HRQ	Helping Relationship Questionnaire
HSC	Hayling Sentence Completion Task
ICD	International Classification of Diseases and Related Health Problems
IGT	Iowa Gambling Task
MDD	Major Depressive Disorder
MI	Metacognitive Index
MRC	Medical Research Council
NNT	Non-Specific Neurocognitive Training
MOCI	Maudsley Obsessive-Compulsive Inventory
OCD	Obsessive Compulsive Disorder
OCI	Order of Construction Index
RASP	Regional seksjon spiseforstyrrelser (Regional Department for Eating Disorders)
RCFT	Rey Complex Figure Test
RCT	Randomized Controlled Trial
RSES	Rosenberg Self-Esteem Scale
SD	Standard Deviation
SI	Style Index
STAI	State Trait Anxiety Scale
TCI	Temperament and Character Inventory
TMT	Trail Making Test
ToL	Tower of London
TSPE	Therapy Suitability and Patient Expectancy
VFT	Verbal Fluency Test
WAIS	Adult Intelligence Scale
WASI	Wechsler Abbreviated Scale of Intelligence
WCST	Wisconsin Card Sorting Test
WHO	World Health Organisation
WISC	Wechsler Intelligence Scale for Children

## ABSTRACT

Cognitive remediation therapy (CRT) is a novel treatment for individuals suffering from anorexia nervosa (AN). The treatment focuses on the process of thought, and aims to raise awareness of how cognitions and behaviors characterised by rigidity and preoccupation with details, common in AN, can be altered through practice and metacognitive techniques. In keeping with the Medical Research Council's framework for systematically evaluating complex interventions, this doctoral thesis presents results from a feasibility trial of CRT for 20 female adolescents with AN, investigating rates of recruitment and retention, treatment delivery and assessment methods. The first paper is descriptive in its nature, and investigates various aspects of treatment delivery and factors associated with recruitment of patients, and treatment adherence. The second paper reports the investigation of the technicalities of assessing changes associated with CRT using psychological and neuropsychological methods and measures. The third paper describes the evaluation of a novel mode of CRT assessment: patient and parental self-reports, and delineates discrepancies between patients and parents in terms of executive function and dysfunction. The results from this dissertation indicate that CRT is feasible for adolescents with AN. However, further investigations are warranted to refine methodology prior to the initiation of a randomised controlled trial.

## LIST OF PUBLICATIONS

### Paper I

Dahlgren, C.L., Lask, B., Landrø, NI & Rø, Ø. (2013). Developing and Evaluating Cognitive Remediation Therapy for Adolescents with Anorexia Nervosa: A Feasibility Study. *Clinical Child Psychology and Psychiatry*. [Epub ahead of print]. DOI: 10.1177/1359104513489980

### Paper II

Dahlgren, C.L., Lask, B., Landrø, NI & Rø, Ø. (2013). Neuropsychological Functioning in Adolescents with Anorexia Nervosa Before and After Cognitive Remediation Therapy: A Feasibility Trial. *International Journal of Eating Disorders*. 46(6):576-81. DOI: 10.1002/eat.22155.

### Paper III

Dahlgren, C.L., Lask, B., Landrø, NI & Rø, Ø. (2013). Patient and Parental Self-Reports of Executive Functioning in a Sample of Young Females with Anorexia Nervosa Before and After Cognitive Remediation Therapy. *European Eating Disorders Review*. [Epub ahead of print]. DOI: 10.1002/erv.2265.

## INTRODUCTION

In recent years, there has been a substantial increase in studies investigating the impact of neuropsychology on eating disorder aetiology, maintenance, and recovery. Clinical neuropsychology examines the relationship between brain pathology and behaviour, and in anorexia nervosa (AN), the focus has been primarily to establish the extent to which weaknesses in cognitive flexibility (i.e. the inability to shift or change mental and behavioural strategies) and central coherence (i.e. the preoccupation with details at the cost of global/contextual processing) contribute to the development of the illness, its perseverance and the likelihood of recovery. Early neuropsychological studies and clinical observations of adult females with AN laid the groundwork for the development of cognitive remediation therapy (CRT), an intervention specifically tailored to remedy weaknesses in these two domains. During the preparatory phase of this doctoral thesis, clinical neuropsychological features resembling those of adults (i.e. rigidity and preoccupations with details) were recurrently reported by clinicians working with younger patients with AN (Fitzpatrick, Darcy, Colborn, Gudorf, & Lock, 2012). However, at that time, research evidence did not support a neuropsychological profile equivalent to that of adult patients, and naturally, treatment studies designed to explore the potential of alleviating such clinical characteristics (such as CRT) were not conducted in this patient group.

The three papers included in this thesis set out to broaden our understanding of the applicability of CRT for young patients with AN, and in particular, its *feasibility*. By adopting the Medical Research Council (MRC) framework for developing and evaluating randomised controlled trials (RCT's) for complex interventions (Craig et al., 2008), our primary objective was to systematically evaluate the various components of our feasibility trial to be able to advocate for either a refinement of the study design, or to propose a subsequent full scale intervention evaluation (e.g. a RCT). This introductory chapter will provide a general background of eating disorders, and especially AN, the diagnosis of interest in this doctoral dissertation. It will also aim to briefly describe the historical development of CRT, and lists an overview of all research studies on its applicability to AN published between August 2005 and November 2013.

## What Are Eating Disorders?

Eating disorders (ED) are manifested by disturbed eating behaviours, excessive preoccupation with weight and shape, body dissatisfaction/distortion, as well as compensatory behaviours such as restrictive food intake, excessive exercise and vomiting to achieve weight loss. They are accompanied by major effects on both physical and mental health. During the last two decades, two standard classification systems have been commonly used to diagnose EDs, the International Classification of Diseases and Related Health Problems – 10<sup>th</sup> Revision (ICD-10) (World Health Organisation, 1992) and the Diagnostic and Statistical Manual of Mental Disorders – 4<sup>th</sup> Edition (DSM-IV) (American Psychological Association (APA), 1994). However, the most common definitions at the time of the research published in this dissertation, are those based on the diagnostic criteria found in the DSM-IV, which outlines three different clinical entities; *anorexia nervosa* (AN), *bulimia nervosa* (BN) and a residual group with distorted eating behaviours that does not meet diagnostic criteria for either AN or BN; *eating disorders not otherwise specified* (EDNOS). Patients included in the three studies presented in this doctoral thesis were all diagnosed with, and in treatment for, AN. Worth mentioning is that a fifth edition of the DSM, the DSM-5, was published in May 2013. This revised version had a number of changes to the eating disorders previously described in the DSM-IV. However, since this doctoral thesis was initiated in January 2011, a little more than 2 years prior to the publication of the DSM-5, definitions and criteria for AN outlined in DSM-IV are used (see **Table 1**).

<b>Table 1. Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV)</b>
<b>Diagnostic Criteria: 307.1 Anorexia Nervosa</b>
A. Refusal to maintain body weight at or above a minimally normal weight for age and height, for example, weight loss leading to maintenance of body weight less than 85% of that expected, or failure to make expected weight gain during period of growth, leading to body weight less than 85% of that expected. B. Intense fear of gaining weight or becoming fat, even though underweight. C. Disturbance in the way one's body weight or shape is experienced, undue influence of body weight or shape on self evaluation, or denial of the seriousness of the current low body weight. D. In postmenarcheal females, amenorrhea, i.e., the absence of at least 3 consecutive menstrual cycles. A woman having periods only while on hormone medication (e.g. estrogen) still qualifies as having amenorrhea.
<i>Restricting Type:</i> During the current episode of Anorexia Nervosa, the person has not regularly engaged in binge-eating or purging behaviour (self-induced vomiting or misuse of laxatives, diuretics, or enemas). <i>Binge Eating/Purging Type:</i> During the current episode of Anorexia Nervosa, the person has regularly engaged in binge-eating or purging behaviour.

## **Anorexia Nervosa**

Anorexia nervosa (AN) is a multifaceted psychological disorder characterized by pathological eating behaviours. It is a serious condition and in some cases, even life threatening (Arcelus, Mitchell, Wales, & Nielsen, 2011) with significant psychological and physical co-morbidity, and poor quality of life (Halvorsen & Heyerdahl, 2006; Keilen, Treasure, Schmidt, & Treasure, 1994). Symptoms of the illness most commonly occur in early to late adolescence, which has an incidence rate of 0.5-0.7% among adolescent females between 15 and 19 (Hoek & van Hoeken, 2003). The DSM-IV describes the core symptoms as refusal to maintain a healthy body weight, intense anxiety about eating, a determined pursuit of becoming thinner, and distorted experiences of one's own body. Methods applied to achieve weight loss and maintain a low body weight encompass refusal to eat and purging behaviours such as excessive exercise, misuse of laxatives and diuretics and vomiting. For adults, the minimum level of severity is based on current body mass index (BMI) (i.e. weight for height ratio) derived from World Health Organization categories for thinness. According to the DSM-IV, diagnostic weight criteria is met when an individual displays a body weight less than 85% of that expected (expected body weight [EBW]), whereas the ICD-10 operates with a diagnostic weight criteria of BMI 17.5 or below. For children and adolescents, age and gender norms are used to calculate EBW, yielding a BMI percentile, which is recommended for use in for both clinical, and research purposes (Le Grange et al., 2012). BMI percentile levels below 10 % is considered being representative of the level of under nourishment often seen in patients with AN (Hebebrand, Himmelman, Hesecker, Schäfer, & Remschmidt, 1996), and BMI percentiles at or below 2.5% warrant paediatric hospital admissions for somatic observation (Statens helsetilsyn, 2000).

### *Aetiology*

The aetiology of AN is complex, largely due to its multifactorial nature. Media influences promoting zero-size body ideals are undoubtedly main contributors to the unhealthy image of what women should look like today, a phenomenon that is predominantly seen in Western societies (Fairburn & Harrison, 2003). However, although such socio-cultural pressure to be thin is likely to have a significant impact on teenagers in their vulnerable period of pubertal development, predisposing biological and psychological factors may render an individual susceptible to AN, and precipitating factors such as stress, poor coping strategies and limited

social support may act as maintaining factors throughout the course of the illness (Schmidt, 2003). Evidence of heritability has been proven in a number of studies where prevalence has been reported being significantly higher in relatives of individuals with eating disorders (Bulik & Tozzi, 2004; Lilenfeld et al., 1998). Also, sibling studies have yielded evidence of an interaction effect of genetic and developmental contributions to the illness (Klump, Burt, McGue, & Iacono, 2007), as well as shared cognitive weaknesses (Tenconi et al., 2010). The unique contribution of cultural, genetic, psychosocial and developmental factors, and the process through which triggers and maintaining factors contribute to the onset of the illness and its perpetuation, is still unknown. Nevertheless, it is important to be aware of, and consider the mediating or moderating capacities of these factors in the treatment of the illness.

### *Comorbidity*

The presence of comorbid disorders in AN is common (Steinhausen, 2002) and may precede the disorder, or emerge as a result of it. Most literature suggest that additive psychiatric disorders complicates both the course and outcome of AN (Casper & Jabin, 1996; Wonderlich, Lilenfeld, Riso, Engel, & Mitchell, 2005), and understanding the extent to which comorbidity effect the individual, the course of the illness and the likelihood of recovery is crucial when treating patients with AN. Multiple studies report elevated rates of depression in patients with AN (Abbate-Daga et al., 2011; Herzog, Keller, Sacks, Yeh, & Lavori, 1992) and major depressive disorders (MDD) has been reported as one of the most common psychological disorders associated with the illness (Godart et al., 2007; Kaye et al., 2008). In addition, high prevalence of anxiety disorders are also common in this patient group (Swinbourne et al., 2012), and rates of obsessive compulsive disorder (OCD) are found to be considerably higher in AN samples than compared to the general population (Altman & Shankman, 2009; Kaye, Bulik, Thornton, Barbarich, & Masters, 2004; Sansone & Sansone, 2011). Further, a number of research studies have reported anxious/avoidant personality disorder (PD) (Diaz-Marsa, Carrasco, & Saiz, 2000; Godt, 2008) and dependent PD (Salbach-Andrae et al., 2008) as being the most common PD in individuals with restricting AN. Personality subtypes of AN have been identified in Lavender et al.'s study (2013) and in Abbate-Daga's study (2011), supporting PD heterogeneity in individuals with AN. In adolescent samples, comorbidity rates are considerably lower than in adults (Bühren et al., 2013), but clinicians should nevertheless be familiar with the risks associated with these

disorders as they represent unfavourable prognostic factors (Salbach-Andrae, et al., 2008), and may serve as triggers as well as maintaining factors.

### *Treatment*

Current treatments for AN often involve both somatic and psychological components. In severe cases, initial treatment efforts often aim for medical stabilization, addressing the potential life threatening physiological effects of starvation and purging behaviours such as electrolyte disturbances, nutritional deficiencies, and cardiovascular and endocrine abnormalities. After these have been tended to, the onerous process of weight restoration can begin. Psychological interventions such as cognitive behavioural therapy (CBT), interpersonal therapy (IPT), unspecified supportive psychotherapy or family based therapy (FBT) (only used in the younger population) are usually applied to tackle the psychological components of the illness, often in conjunction with nutritional counselling and physical monitoring. Interdisciplinary treatment in either in- or outpatient settings are often necessary (Steinhausen, Grigoriu-Serbanescu, Boyadjieva, Neumarker, & Winkler Metzke, 2008), and are dependent on the severity of the illness, and the individual need of the patient. Inpatient treatment tends to be more intense and offered during a shorter time span, whereas outpatient treatment is less intense and can have a substantially longer course.

Although previous research in the field of eating disorders has made important contributions to the understanding of AN, there is currently little evidence to support effective treatments for the illness (Fairburn, 2005), and there is no recommended first line treatment (National Institute for Health and Clinical Excellence (NICE), 2004). The evidence base for treatment efficacy in adult AN is scarce, and despite the fact that there are a number of approaches currently applied in the treatment of the illness (e.g. CBT, IPT, cognitive analytical therapy, FBT, nutritional counselling etc.), existing RCT's are limited and sample sizes small (Gardner & Wilkinson, 2011). Also, existing RCT's appear inconclusive as short vs. long-term investigations, sub group phenomena and current state of illness appear to influence treatment outcome, making it difficult to compare studies and predict long-term effects. Further, a recent randomised controlled efficacy trial in adults (the ANTOP- study) failed to find any significant difference in weight gain at the end of treatment when comparing focal psychodynamic therapy, enhanced cognitive behaviour therapy and optimised treatment as usual (Zipfel et al., 2013), rendering it challenging to conclude with one intervention being

superior to the others. For the younger patients, current research evidence suggests that a particular form of family therapy, FBT (Lock, Le Grange, Agras, & Dare, 2001) is the most efficient approach, and that one might achieve recovery rates somewhere between 50 and 80% (Lock, 2010, 2011; National Institute for Health and Clinical Excellence (NICE), 2004).

Although higher recovery rates are reported in adolescents than in adults, it is still unclear whether such rates are effects of the family treatment per se, or if it is due to the fact that adolescents in general show a better prognosis than adults (Fairburn & Bohn, 2005). Also, although FBT is often the preferred choice of treatment for this patient group (Eisler, Simic, Russel, & Dare, 2007; National Institute for Health and Clinical Excellence (NICE), 2004), its superior effect compared to individual therapies has been limited to mild illness (Lock, 2010), and it is still unclear whether the effect of FBT persist in the long-term (Herscovici, 2013), whether the outcome differs with regards to age and chronicity (Russell, Szmulker, Dare, & Eisler, 1987) and the relative importance of the parent-therapist alliance in the recovery process of these young patients (Forsberg et al., 2013). Also, the few existing RCT's are biased towards FBT, and generally, methodologically challenged by small sample sizes, wide age-ranges and high dropout rates.

Recently, a novel approach to treating young patients with AN has emerged; Enhanced Cognitive Behavioural Therapy (CBT-E). CBT-E has been associated with positive outcomes in adults with eating disorders (Byrne, Fursland, Allen, & Watson, 2011; Fairburn et al., 2009; Fairburn et al., 2013), and recently, substantial improvements in both weight and ED psychopathology have been reported also for adolescents with AN (Dalle Grave, Calugi, Doll, & Fairburn, 2013). Although further research is warranted for a fuller understanding of the effects of CBT-E for young patients with AN, this intervention is a welcome addition to the relatively limited scope of treatment options for this patient group, and might serve as a cost-effective alternative to FBT.

### *Prognosis*

The complexity of AN renders it difficult to treat, and the prognosis is relatively poor. Although AN has a lifetime prevalence in the female population around 2-3 % (Favaro, Ferrara, & Santonastaso, 2003; Hoek & van Hoeken, 2003) and hence, is relatively uncommon, it has the highest morbidity and mortality rates of all psychiatric illnesses

(Arcelus, et al., 2011; Smink, van Hoeken, & Hoek, 2012) with suicide being the most common cause of death (Franko et al., 2013; Preti, Rocchi, Sisti, Camboni, & Miotto, 2011). On average, only a little more than one-third (37%) of individuals afflicted recover within 4 years post illness onset (Berkman, Lohr, & Bulik, 2007), and about 50 - 60% make a full and sustained recovery with the rest either remaining symptomatic or relapsing and remitting (Steinhausen, 2002). Dropout rates as high as 50% have been reported for both in- and outpatients (Sly, Morgan, Mountford, & Lacey, 2013), with higher rates indicating lower response to treatment and less favourable outcomes. The prognosis for adolescents with AN is better than that of the adult population, with lower mortality rates (Herpertz-Dahlmann et al., 2001), possibly due to lower drop out of treatment in this patient group (Hubert et al., 2013). Treatment adherence is associated with better outcomes and shorter symptom duration (Crisp et al., 1991; Gowers et al., 2007). Based on this evidence, it is imperative that young females with AN engage in treatment at an early stage of their illness, and that they are encouraged to remain in treatment to achieve desired intervention effects.

### **Anorexia Nervosa and Cognitive Functioning**

Overall, there is considerable recent evidence suggesting an underlying neurodevelopmental component to AN (Rose, Davis, Frampton, & Lask, 2011). In adults, the main findings from neuropsychological studies have revealed consistent weaknesses in both *set-shifting* (Roberts, Tchanturia, Stahl, Southgate, & Treasure, 2007) and *central coherence* (Lopez et al., 2008; Lopez, Tchanturia, Stahl, & Treasure, 2008).

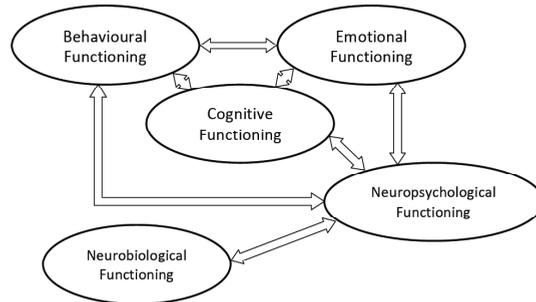
*Set shifting*, or cognitive flexibility, is one of the most important executive functions, and allows for people to shift back and forth between different information units, or “mental sets”. Generally, those who are good at flexible thinking are also good at multi-tasking, and are able continuously to alter their thoughts and behaviours according to shifting environmental demands. Impaired set shifting (sometime referred to as poor cognitive flexibility) refers to difficulties with shifting or changing mental strategies and rules according to changing contextual demands. This inflexibility can manifest as an inability to adapt to changing circumstances, and in difficulty in overriding well-learned cognitive and behavioural patterns. In patients with AN, deficits in this particular domain might lead to concrete and rigid approaches to problem solving, and to the perseverance of maladaptive thinking and behavioural patterns. There is empirical support stating that greater impulsivity (i.e. less

rigidity) is a positive prognostic factor and predict greater likelihood of recovery in patients with AN (Zerwas et al., 2013). Consequently, a person who is able to think flexibly, is probably also more likely to act in accordance with the continuous changing environmental demands, and hence, might be more susceptible to the process of change that any intervention for eating disorders encompasses. Flexibility, set-shifting and multi-tasking therefore play an important role in the recovery process, and should not be neglected in treatment.

*Central coherence* refers to the tendency to process information in terms of the whole gestalt - the big picture - as well as fine detail. The ability to process information globally enables people to perceive themselves and their surroundings as whole, rather than separate, or detached units. Further, this ability also allows for interpretation of details contextually, and gives a fuller understanding of the integration of, and relationship between these. It is an extremely important function in our everyday undertakings, and underlies many of our thoughts and actions both as children, adolescents and adults. Neurocognitive studies exploring central coherence in adult patients with AN have yielded consistent evidence of weaknesses in global processing (Lopez, Tchanturia, Stahl, & Treasure, 2008), and some have also reported superior attention to details (Allen et al., 2012; Fonville et al., 2013; Rose, Frampton, & Lask, 2013). In AN, it appears as though the balance between global and local information processing is disrupted, resulting in an excessive preoccupation with detail, order and symmetry, at the cost of the bigger picture. In relation to the illness, this preoccupation could manifest in a pathological fixation with calorie- and fat content, weight gain- and loss, and detailed exercise routines and practices, all features that perpetuate eating disorder psychopathology.

Various models have been put forth to explain the connection between neuropsychological weaknesses and its cognitive and behavioural manifestations in AN. One of these suggests that underlying neurobiological abnormalities are mediated by neuropsychological functioning to influence cognitive, emotional and behavioural functioning in eating disorders (see **Figure 1**) (Frampton & Rose, 2013). Emaciation not only affects the body but also the brain. However, whereas some report neurocognitive impairments such as weak set-shifting and central coherence reverting to normal with weight gain (Hatch et al., 2010) or being unrelated to BMI (Fowler et al., 2006; Rose, Frampton, & Lask, 2012), others have found they do not normalize with refeeding (Danner et al., 2012; Green, Elliman, Wakeling, & Rogers, 1996; Lena, Fiocco, & Leyenaar, 2004). Also, a number of publications have reported

impaired set-shifting in unaffected family members of patients with AN (Galimberti et al., 2013; Holliday, Tchanturia, Landau, Collier, & Treasure, 2005; Tenconi, et al., 2010) leading researchers to suggest weaknesses such as impaired set-shifting being a trait, rather than a state marker for AN (Kaye, Wierenga, Bailer, Simmons, & Bischoff-Grethe, 2013), and neuropsychological deficits as preceding and underling the eating disorder (see **Figure 1**), rather than as being a result of the illness.



**Figure 1.** Conceptual model for the role of neuropsychological functioning in mediating between underlying neurobiological functioning and psychological functioning (cognitions, behaviours & emotions) in eating disorders (Frampton & Rose, 2013).

Consistent with evidence of weak neuropsychological functioning in adult patient samples, but limited in its empirical support, cognitive weaknesses such as rigidity and preoccupation with details are often observed and reported by clinicians working with younger patients with AN (Fitzpatrick, et al., 2012). However, recent research report mixed findings for impaired set-shifting and central coherence in this patient group. While many studies fail to report weaknesses in these domains (Bühren et al., 2012; Dahlgren, Lask, Landrø, & Rø, 2013b; Fitzpatrick, et al., 2012; Rose, et al., 2012; Rose, et al., 2013; Shott et al., 2012), others reveal inconclusive results (Rose, et al., 2012) subtle- (Stedal, Rose, Frampton, Landrø, & Lask, 2012) or substantial weaknesses (Allen, et al., 2012). Also, contrary to research in adult samples, cognitive impairments have been reported to normalize with weight restoration (Hatch, et al., 2010). Taken together, inconclusive results accentuate the need of reconsidering weaknesses in these domains as predisposing traits, and highlights the necessity of exploring alternative explanations such as rigidity and preoccupation with details being results of illness chronicity (scarring effects), interaction effects between chronicity and underweight and/or malnutrition, or as potential sub group phenomena. Also, studies exploring impairments in these domains in adolescents have largely focused on group level analysis, rendering it possible for individual differences to be missed (Rose, et al., 2012).

It is possible that the relative lack of effectiveness in treatments for AN is due in part to the fact that previous treatments tend to focus on emotions, cognitions and behaviours, but fail to address cognitive weaknesses such as poor set-shifting and an inability to process information in terms of the gestalt (i.e. the big picture, the whole). In patients with AN, it is hypothesized that such weaknesses have undesirable effects in terms of social interactions (Tchanturia, Lloyd, & Lang, 2013), the development of the illness, its maintenance, response to treatment and ultimately, recovery (Bühren, et al., 2012; Danner, et al., 2012; Kanakam & Treasure, 2013; Tchanturia et al., 2011; Tenconi, et al., 2010). Given the complexity of, and relation between, eating disorder cognition and behavior, understanding and treating maladaptive cognitions might serve as a first step in the process towards recovery. CRT is an intervention aimed at improving the weak cognitive characteristics often seen in patients with AN, and the behavioural consequences of these by targeting the neuropsychological functions thought to influence such characteristics.

### **What is Cognitive Remediation Therapy?**

The CRT technique was originally conceptualized and developed as an intervention for patients with brain lesions during the Second World War. Led by the Russian neuropsychologist Alexander Luria (Luria, 1972) a team of researchers made significant advances in the field of brain surgery, and in the restoration of brain functions after trauma. In the search for ways to compensate psychological dysfunction in patients suffering from brain lesions, it was noted that the implementation of simple cognitive and behavioural exercises could rehabilitate neuropsychological deficits in specific brain regions. The pioneering work of Luria laid the groundwork for the development of CRT during the second half of the 20<sup>th</sup> century, but over the last 50 years, the method and its application have been gradually adapted to suit individuals suffering from other health conditions as well. In psychiatry, CRT has been most commonly associated with the treatment of cognitive dysfunction in patients with schizophrenia, and there is an extensive body of published studies describing positive outcomes of CRT for this patient group (e.g. Kurtz, 2012 and Wykes & Spaulding, 2011). The approach has also been successfully used in the treatment of other mental health conditions such as mood disorders (Bowie, Gupta, & Holshausen, 2013), attention deficit hyperactivity disorder (ADHD) (Stevenson, Whitmont, Bornholt, Livesey, & Stevenson, 2002), alcohol dependence (Rupp, Kemmler, Kurz, Hinterhuber, & Fleischhacker, 2012), depression (Bowie et al., 2013; Morimoto, Wexler, & Alexopoulos, 2012) and OCD (Buhlmann et al., 2006).

CRT for AN is a relatively new treatment approach, and focuses on the process of thinking (i.e. the how) rather than the content (i.e. the what). In contrast to traditional interventions that centre on increasing food intake and on addressing ED specific symptoms such as weight and shape concerns, CRT aims neither to address nor treat these. The focus is primarily to decrease rigidity (i.e. increase flexibility) and achieve a balance between local (detailed) and global (the bigger picture) information processing strategies. By motivating the patient to engage in metacognitive processes, that is, to consider their cognitive/thinking styles and explore alternative strategies, the goal is for the patient to be able to alter inefficient thought and behavioural patterns.

The very first paper on CRT for AN was published in 2005 (Davies & Tchanturia, 2005), and reported results from a single case study illustrating the use of CRT for an adult female inpatient refusing to participate in any of the core treatment approaches at the inpatient unit where she was admitted. The materials used were hand picked from the set-shifting module in Delahunty & Morice's (1993) "*A training programme for the remediation of cognitive deficits in schizophrenia*", and gradually thereafter, novel materials were developed and assembled in CRT manuals specifically tailored to remediate cognitive weaknesses in females with AN (Tchanturia & Davies, 2010; Tchanturia, Davies, Reeder, & Wykes, 2010). Research on CRT for AN is evolving rapidly, and is currently transforming from feasibility and piloting trials into the realm of what is considered to be the gold standard when it comes to testing the effect of a specific treatment approach - RCT's.

Alongside study design transformations, the aim of delivering CRT, and contributions thought to be associated with the intervention, appear to have changed. CRT was initially hypothesized to motivate and engage patients in subsequent therapeutic interventions, but during the course of its development and adaptation, the range of outcome measures used has expanded considerably, and now also includes assessments of neuropsychological functioning, eating disorder psychopathology, comorbidity, perfectionism, treatment attrition and comparisons to other neurocognitive interventions. As knowledge of the applicability of CRT for AN has accumulated during almost a decade, such knowledge has now guided two recent RCT's, and all evidence points in the direction of additional RCT's being carried out in a near future. As an essential step to evaluate research published on CRT and AN, and to obtain an overview of the different characteristics of studies published in this field, a literature review was performed. The next section of the thesis reviews progress in the development of

CRT for AN between August 2005 and November 2013, and summarizes published research studies within this time frame.

## **Literature Review**

Restricted to the aim and scope of the doctoral thesis, the literature was reviewed using the PubMed, Web of Knowledge and PsycINFO search terms “cognitive remediation therapy” AND “anorexia nervosa”. The PubMed search yielded 25 publications, Web of Knowledge 18 publications and PsycINFO 19 publications. Together, the three searches yielded 62 publications, which were cross-referenced. 34 individual publications were identified. Publication titles and abstracts were screened initially, and eligibility was established by reading the full texts. After duplicates had been omitted, a manual reference search was conducted to investigate additional papers. Two additional papers were identified during this search. On the basis of the inclusion criteria outlined below, 21 were identified as relevant, and selected for review. The main characteristics of these studies are presented in **Table 2**.

### *Inclusion Criteria:*

- 1) Studies of any design focusing on cognitive remediation therapy and AN
- 2) Articles that were written in English or had an available published English translation
- 3) Articles that had been published in peer reviewed journals

### *Excluded Studies*

All in all, 17 publications were excluded from the review. Two publications appeared twice in the same PubMed search (Genders & Tchanturia, 2010; Pitt, Lewis, Morgan, & Woodward, 2010), one study was excluded as it was written in Polish (Cwojdzinska, Markowska-Regulska, & Rybakowski, 2009), and another study was omitted as it had been published as a meeting abstract rather than in an article format (Vorgaft & Bercovich, 2012). Six studies were excluded as these did not focus specifically on CRT for AN (Fagundo et al., 2013; Fonville, et al., 2013; Guardia, Luyat, & Cottencin, 2011; Hay, Touyz, & Sud, 2012; Nunn, Frampton, Fuglset, Torzsok-Sonnevend, & Lask, 2011; Safer & Chen, 2011), and 5 publications were excluded as these represented either books or book chapters rather than peer reviewed papers (Adan & Kaye, 2011; Fox & Goss, 2012; Grilo & Mitchell, 2010; Lopez,

Davies, & Tchanturia, 2012; Tchanturia & Hambrook, 2010). Finally, two studies evaluating the combination of CRT and emotional skills training (CREST) (Davies et al., 2012; Money, Genders, Treasure, Schmidt, & Tchanturia, 2011) were excluded from the review as the design of these studies did not allow for assessment of CRT specific contributions. As mentioned earlier, 21 papers were reviewed. Three of these papers (Dahlgren, Lask, Landrø, & Rø, 2013a; Dahlgren, et al., 2013b; Dahlgren, Lask, Landrø, & Rø, 2013c) are based on the same sample. The author is not aware of additional sample overlaps.

### *Overview of Included Studies*

The twenty-one reviewed studies were published between September 2005 and November 2013, with sample sizes ranging from 1 to 46 participants, and ages ranging from 12-62. With the exception of five male participants, all patients included in the studies were female, and the vast majority of participants were diagnosed with AN. One study had included patients with a current diagnosis of AN plus recently recovered AN patients (Pitt, et al., 2010), and another study had included both current AN patients as well as participants with an EDNOS diagnosis (Pretorius et al., 2012). Out of the 21 studies reviewed, two reported results from RCT's, both published in 2013 (Brockmeyer et al., 2013; Lock et al., 2013). Participants in the included studies were currently enrolled in either in- or outpatient treatment for their eating disorder, and all received CRT as a conjunctive intervention. Included studies varied widely, for example according to whether CRT was delivered individually, in groups or families, the number of sessions offered, the intensity of these and the materials used. Studies also varied according to the aim of the study and consequently, what outcome measures were applied. Methodological issues in comparing studies were identified in terms of sample sizes, the choice of outcome measures and statistical methods used. Six different types of studies were identified:

- 1) Single case studies (n=3)
- 2) Feasibility studies (n=6)
- 3) Studies assessing pre and post CRT functioning without using control groups (n=4)
- 4) Theoretical/Empirical papers (n=2)
- 5) Additive/Combined Studies (n=4)
- 6) Randomised Controlled Trials (n=2)

### *1) Single Case Studies*

The three single case studies (Davies & Tchanturia, 2005; Pretorius & Tchanturia, 2007; Tchanturia, Whitney, & Treasure, 2006) represent the very beginning of the development of CRT for AN. All papers describe a single, adult female inpatient with longstanding AN, undergoing 10 sessions of individual CRT. The three papers neatly illustrate how the CRT materials were adopted and adapted from the set-shifting module from Delahunty and Morice's (1993) work with schizophrenic patients, and how this material became the corner stone in the development of the CRT for AN materials that most clinicians and researchers use today. The earliest of the three papers (Tchanturia, Campbell, Morris, & Treasure, 2005) emphasises the importance of bridging the gap between in-session task performance and its relevance to everyday undertakings, a crucial part of CRT which has been adhered to in the majority of subsequent studies. In the most recent of the three case studies (Pretorius & Tchanturia, 2007), the concept of behavioural tasks (in subsequent studies often referred to as homework) is introduced as a part of the therapeutic work with the patient, aiming to facilitate the implementation of newly learned strategies to every day life situations. The most recent case study is descriptive in its nature and focuses on the patients experience with CRT. Results from this study were promising in terms of CRT's potential in increasing the effectiveness of other interventions, and with regards to the development of a heightened awareness of the patient's thinking style. The two former papers set out to investigate changes in neuropsychological functioning and clinical variables during the course of the intervention, and were identical in terms of outcome measures used. Results were inconclusive in that some performance measures had improved whereas others had not. However, care is required when interpreting results derived from single case studies, as they are not generalizable. However these papers are useful in illustrating the rationale for delivering CRT to patients with AN, and the clinical implications of the implementation of CRT on an individual basis, but should not be interpreted as evidence of the effect of CRT on eating disorder psychopathology, co-morbidity and neuropsychological functioning.

### *2) Feasibility Studies*

Six feasibility studies (Dahlgren, et al., 2013a; Easter & Tchanturia, 2011; Lask & Roberts, 2013; Whitney, Easter, & Tchanturia, 2008; Wood, Al-Khairulla, & Lask, 2011; Zuchova, Erler, & Papezova, 2013) were identified amongst the twenty-one papers. All studies

investigated CRT for patients with AN, but the diversity of sample compositions (sample size, age, in- and/or outpatients), intervention approaches (individual, family or group, treatment intensity, intervention materials) and outcome measures (qualitative or quantitative) rendered it difficult to compare studies and to generalize findings. Three papers reported results from patient feedback letters (Whitney, et al., 2008; Wood, et al., 2011; Zuchova, et al., 2013) with the two latter supporting the feasibility of CRT delivered in a group format, and the former when delivered individually. These three studies investigated feasibility for patients ranging widely in ages (13-54), which strengthen the applicability of CRT across ages, and support the feasibility of the intervention at various stages of illness and developmental trajectories. The Wood et al. study (2011) is the first to explore CRT for adolescents with AN, and it is also the first paper to present a detailed outline of the specific task(s) used each session. Results yielded evidence of feasibility and patient satisfaction, but also feedback on some of the drawbacks of delivering CRT in a group format.

In 2013, the second paper exploring CRT for adolescents with AN was published. This time, the format of delivery had changed, and the 20 patients in the Dahlgren et al. study (2013a) received individually delivered CRT, tailored to meet each patient's specific needs. The individual tailoring was described as a strength in this study, and as an advantage compared to group CRT in that it allowed for each patient to focus on her particular weakness(es). This was also the first study to use materials developed specifically for children and adolescents (Lindvall, Owen, & Lask, 2010), and the very first materials that were published (online) and freely accessible to the public. The study published by Easter and Tchanturia (2011) illustrates a novel approach to feasibility in its application of therapist's feedback letters to examine how CRT has been implemented in the daily life of the patients. It is pioneering and unique in its attempt at establishing a more ecologically valid interpretation of how CRT has affected the daily life of the patients, and used a new methodology to do so. No subsequent studies have used this type of methodology, although many report using therapist feedback letters. The most recent feasibility study explores the use of CRT when used in family settings (Lask & Roberts, 2013), and reports clinical and observational data to illustrate its use in this novel mode of delivery. Overall, these six studies supports the feasibility of CRT across ages, illness severity, current treatment engagements and when delivered in various formats. However, many of these papers are limited in their description of the intervention, rendering it difficult to determine the specific content of the CRT sessions. Also, as the intervention was not standardized, it is uncertain whether the patients were actually receiving the same type of

CRT, or if the variation in intervention designs and content renders it impossible to compare outcomes.

### *3) Assessment of Pre and Post CRT Functioning*

The four studies investigating pre and post CRT functioning without using control groups (Abbate-Daga, Buzzichelli, Marzola, Amianto, & Fassino, 2012; Dahlgren, et al., 2013b, 2013c; Tchanturia et al., 2008) illustrate how the use of a wide variety of outcome measures have been applied to investigate changes across the intervention span. These include eating disorder psychopathology, comorbidity, impulse regulation, executive functions (including cognitive flexibility and decision-making), central coherence, and overall functioning. All but one study describe CRT given as a adjunct to inpatient (vs. outpatient treatment) treatment, and patients appear to have received approximately the same number of sessions (about 10). However, contrasting features are far more common, and concern the age of the participants, treatment intensity, the CRT materials used, and the choice of assessment instruments. It is thus not surprising that results diverge with regards to neuropsychological functioning post CRT as different instruments and different aspects of the same measure have been used to evaluate test performance after treatment. For example, both Tchanturia et al. (2008) and Abbate-Daga et al. (2012) found significant changes in Trail Making Test (TMT) performance in adult patients with AN, whereas Dahlgren et al. (2013b) did not in their sample of adolescents. However, in these three studies a variety of assessment methods were used and both TMT shifting time, number of preservative errors, total completion time and attention were recorded, rendering it difficult to compare results.

Three studies (Dahlgren, et al., 2013b, 2013c; Tchanturia, et al., 2008) (of which the two former are based on the same sample) report a decrease in depression post CRT, with one of them (Dahlgren, et al., 2013b) challenging the previously held notion that weight restoration alone does not significantly contribute to changes in neuropsychological functioning (Tchanturia, et al., 2008). Further, the two studies published by Dahlgren et al. (2013b and 2013c) are pioneering in addressing methodological issues previously ignored such as test-retest effects and biases associated with the absence of proper controlling and corrections for multiple comparisons. The assessment method used in Dahlgren et al. (2013c) highlights a novel approach to investigating post CRT functioning. As the first of its kind in using a validated self-report measure, the authors compare patient and parental reports of executive

functioning (EF) post CRT. On a group level, conclusions point in the direction of scores within the normal range, but case analyses reveal substantial discrepancies between parents' and patients' ratings of EF, and substantial individual differences within the group. Because of the preliminary nature of these four studies, and the great variety amongst them, it is difficult to compare and generalize findings. Methodological challenges such as short test-retest intervals and the associated risk of learning effects, the use of identical pre- and post-CRT assessment instruments, generally weak statistical analyses and the lack of control groups renders it impossible to conclude whether observed changes (or the lack of these) are direct results of the intervention itself, or associated with other factors such as changes in comorbidity, eating disorder psychopathology or weight.

#### *4) Theoretical/Empirical Papers*

In the time period 2005-2013, two papers have sought to summarize the current evidence of CRT for AN, and its future in research and clinical practice (Baldock & Tchanturia, 2007; Tchanturia, et al., 2013). The first paper was published in 2007, merely two years after the first case study had been published, and aimed to review the empirical foundations of CRT and its function for this patient group. The authors also provided the readers with a speculative view of how CRT would be further developed during the next ten years, and predicted i) improvement of intervention designs, ii) tailored CRT based on neuropsychological and clinical profiles iii) effectiveness in both severe and mild cases of AN and iv) delivery in both in- and outpatient settings. In this paper, the central function of CRT for AN is described as to improve the basic process of thought, and more specifically, set-shifting and global information processing (i.e. central coherence). Further, the focus on cognitive processes (as opposed to cognitive content), and learning new thinking strategies (rather than practising a specific skill) through metacognition, are outlined as being important aspects of increasing concentration, boosting self-esteem, and as a facilitator in pre-treatment, or an add-on treatment for CBT, a topic that was recently revisited in the RCT conducted by Lock et al. (2013).

The second paper is one of the latest papers to be published on CRT for AN, and aims to delineate current evidence and future directions of CRT for this patient group. The paper contains a summary of published studies reporting CRT in AN, but as the 9 studies described here overlap with papers in the literature review presented in this thesis (see **Table 2**), no further attention will be paid to these here. However, several suggestions for future research

directions are put forth, amongst these broadening the understanding of neuropsychological functioning in adolescents with AN, direct intervention comparisons (including CRT), the role of cognitive improvement on ED symptomatology and the involvement of family members and carers in CRT, a theme recently accentuated in the feasibility study by Lask & Roberts (2013).

##### *5) Additive/Combined Studies*

We identified four published studies with a distinct overlap with regards to feasibility and pre- and post-CRT assessments (Genders & Tchanturia, 2010; Pitt, et al., 2010; Pretorius, et al., 2012; Tchanturia, Davies, & Campbell, 2007). The earliest of these four studies was published in 2007 (Tchanturia, et al., 2007), and although using a very small sample size (N=4), it represents the transition from the single case study format, to a novel study design where larger groups of patients are included, and where authors have set out to investigate both feasibility and neuropsychological performance before and after the intervention. Significant changes in set-shifting and patient feedback from this study were used to further develop CRT for patients with AN. Also, results from this study led to the refining of materials, and the inclusion of behavioral tasks in the updated (in-house) manual produced a few years later (Tchanturia & Davies, 2010).

Group CRT was first described and evaluated in the study by Genders & Tchanturia (2010), and similar to the Tchanturia et al.'s work from 2007, this study also sought to combine knowledge of feasibility and changes post-CRT. However, this time a novel format of delivery was applied, the group format. Results supported acceptability for both patients and group facilitators, and a heightened rate of self-reported ability to change was reported by the patients. However, no significant changes in cognitive flexibility or self-esteem were reported, leading to the inevitable discussion of the extent to which one can expect changes after merely four sessions, and potential gains of adding extra sessions. When the third group-CRT paper was published in 2012 (Pretorius, et al., 2012), tasks had been adapted from the Genders & Tchanturia study (2010), but to accommodate patients who were already engaged in an intense six-week programme, no more than 4 sessions were offered. Again, similar to the previous group CRT study, results supported the acceptability of the intervention, but did not support significant changes in self-reported flexibility.

In 2010, Pitt et al, made an important addition to the field in not only exploring the feasibility through patient feedback, but by introducing a novel CRT outcome measure; perfectionism. And as the first of its kind, this study also provided data based solely on outpatient assessments. Similar to the data reported in Tchanturia et al. (2007), self-reported flexibility was significantly higher post-CRT. In terms of perfectionism, results could not be calculated statistically due to the small sample (N=7), and trends were inconclusive as both increases and decreases in scores were observed.

#### *6) Randomised Controlled Trials*

The two most recent papers published on CRT for AN are both RCT's, and represent a giant leap from that of feasibility and case studies in terms of the possibility of measuring intervention effects. The first of these studies (Lock, et al., 2013) explored the role of CRT in reducing attrition in RCT's for AN. In this study, 46 patients with AN were randomized to receive either eight sessions of CRT or CBT over a period of 2 months. Following these initial eight sessions, both groups received 16 CBT sessions over a period of 4 months. For patients receiving CRT, results revealed lower dropout rates compared to the CBT group (13 and 33 % respectively), as well as significant changes in set-shifting and central coherence at the end of the intervention. However, dropout rates were obtained through data collected at the main outcome point (session 8), after which the rate of attrition increased in the CRT group and eventually, rose to a level matching that of the CBT patient group. Also, no significant differences between CRT and CBT groups in outcome measures such as weight or ED psychopathology were observed at the end of treatment. It thus appears that CRT may have to be delivered alongside an additional intervention (not merely previously to) for the attrition effect to be operative. In addition, results indicate that CRT has an effect on specific neurocognitive functions, but shows no superiority in terms of improving ED symptomatology compared to CBT.

The most recent RCT (Brockmeyer, et al., 2013) introduces a novel approach to CRT; face-to-face sessions *plus* computer assisted homework. Data from 25 treatment completers, 11 receiving CRT focusing specifically on cognitive flexibility, and 14 receiving non-specific neurocognitive therapy (NNT) were analysed. Patients in both groups received 30 sessions of which 9 were administered face-to face. The remaining 21 sessions were comprised of computer-assisted homework. In contrast to the Lock et al. (2013) study, no significant

difference in treatment adherence was observed. However, in line with Lock et al., Brockmeyer et al. (2013) also found changes in cognitive flexibility being significantly higher in the group receiving CRT, than in the control group (i.e. in the group receiving NNT).

To sum up these two studies, it appears as though CRT is efficient in improving specific neurocognitive functions. However, whereas the Locke et al. (2013) failed to find evidence of weight and comorbidity as moderators for treatment response, Brockmeyer et al. (2013) did not investigate such associations, which previously have been reported having significant effects on cognitive functioning post CRT (Dahlgren, et al., 2013b, 2013c). The potency of CRT with regards to improvements in eating disorder psychopathology and comorbid psychiatric illnesses thus still remains unclear, and larger randomized controlled trials are needed to further address this issue. Also, the mode of delivery in the two RCT's differed substantially, indicating that different forms of the therapy were offered to the patients. Therefore, interpretation of results should be viewed as specific to each study rather than general, and comparisons should take into account the variation in study designs, mode of treatment delivery, choice of outcome measures and patient characteristics.

**Table 2. Characteristics of included studies**

Author (date)	Aim of Study	Outcome Measures	Sample Size	Patient Diagnosis	Sample Age/Range (Mean)	Setting	Mode of Delivery	Number of Sessions	Intensity	Intervention Materials	Outcomes
Abbate-Daga et al. (2012) <sup>3</sup>	To measure the effect of CRT on cognitive flexibility	BMI, EDI-2, BDI, GAF, WCST, IGT, TMT, HSCST	20	AN	(22.5)	Out	Individual (FIT)	10	Once Weekly	An Italian version of Tchanturia et al.'s CRT manual	Improved neuropsychological performance. Significant improvement in impulse regulation, interoceptive awareness, reflexive skills and awareness.
Brockmeyer et al. (2013) <sup>6</sup>	To investigate feasibility and efficacy of specifically tailored CRT, compared to non-specific neurocognitive training (NNT)	Cognitive Set-Shifting	25 (11*/14)	AN	(23.6*/26.7)	In & Out	Computer assisted & Individual (FIT)	30	30 sessions over 3 weeks	Modified version of the original manual & computer assisted homework*	Participants receiving CRT outperformed participants in the NNT condition in cognitive set-shifting. Both groups showed high treatment acceptance.
Baldock & Tchanturia (2007) <sup>4</sup>	To describe the foundations, functions and future of CRT for AN	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	Predictions of future improvements in treatment design, effective for both severe and mild cases of AN in both in- and outpatient settings and individually tailored.
Dahlgren et al. (2013a) <sup>2</sup>	To assess the feasibility of CRT for children and adolescents with AN	Feasibility: Recruitment and retention, delivery, materials, clinical experiences	20	AN	13-18 (15.9)	In & Out	Individual (FIT)	7-12	Once or twice weekly	The CRT Resource Pack	Results indicate feasibility for young patients with AN with regards to recruitment, materials, individual tailoring and delivery, and clinicians.
Dahlgren et al. (2013b) <sup>3</sup>	To assess neuropsychological functioning pre and post CRT	BMI Percentiles, EDE-Q, BDI-II, STAII, the Ravello Profile	20	AN	13-18 (15.9)	In & Out	Individual (FIT)	7-12	Once or twice weekly	The CRT Resource Pack	Significant changes in weight, depression, visio-spatial memory, global information processing and verbal fluency. Changes in weight had a significant effect on improvements in visuo-spatial memory and verbal fluency.
Dahlgren et al. (2013c) <sup>3</sup>	To explore self-reports and parental ratings of executive function before and after CRT	EDE-Q, BDI-II, STAII, BRIEF-SR and BRIEF-PF	17	AN	13-18 (15.9)	In & Out	Individual	7-12	Once or twice weekly	The CRT Resource Pack	Decrease in the BRIEF-SR shift subscale post CRT. Parent reports revealed significant lower scores on the shift, emotional control and working memory subscales, and on two composite indices. Substantial discrepancies between patients' and parent's ratings.
Davies & Tchanturia (2005) <sup>1</sup>	To illustrate how CRT can be used to stimulate mental activities and improve thinking skills in acute AN	MOCI, HADS, TMT, Brixton Test, Cat Bat, the Uzmadze Illusion Task	1	AN	21	In	Individual (FIT)	10	Two 3 weekly + two twice weekly sessions	The shifting module developed for schizophrenia by Delahunty & Morice (1993)	Improvement in cognitive set-shifting.
Easter & Tchanturia (2011) <sup>2</sup>	To examine how CRT has been implemented in the daily life of the patients through therapists' feedback letters	Therapist Feedback Letters	26	AN	Adults	In	--	10	Twice weekly	A manual described in Easter & Tchanturia (2011)	Feedback letters were positive and motivational, and highlight difficulties in patients' metacognitive abilities, and difficulties in relating CRT to everyday activities.
Genders & Tchanturia (2010) <sup>5</sup>	To report CRT development and acceptability in a group format	CFS, RSE, Motivational Ruler	30 (2 male)	AN	14-62	In & Out	Group (FIT)	4	Once weekly	Tasks focusing on cognitive flexibility & multi-tasking	Statistically significant gains in self-reports of ability to change. CRT was found to be acceptable, useful and positive by both patient and group facilitators.

**Table 2. Continued**

Author (date)	Aim of Study	Outcome Measures	Sample Size	Patient Diagnosis	Sample Age/Range (Mean)	Setting	Mode of Delivery	Number of Sessions	Intensity	Intervention Materials	Outcomes
Lask & Roberts (2013) <sup>2</sup>	To assess feasibility of CRT in family settings	Clinical Observation	4	AN	14-19	In & Out	Family (FtF)	1-6	Varying from weekly to monthly	The CRT Resource Pack	CRT is useful when applied in families, and authors suggest a subsequent formal evaluation of this mode of delivery.
Lock et al. (2013) <sup>6</sup>	To evaluate the feasibility of using CRT to reduce attrition in RCT's for AN	Attrition, weight, EDE, TSPE, HRQ, WAI-SIII, D-KEFS, RCFT, WCST	46 (23*/23)	AN	(22.7)	Out	Individual (FtF)	8*	8 session during 2 months*	Materials described in Tchanturia & Lock (2011)*	CRT is acceptable and feasible for use in RCT's. It may also reduce short-term attrition.
Pitt et al. (2010) <sup>5</sup>	To evaluate the benefit of CRT in terms of changes in self-reported perfectionism and patient feedback	FMDPS, Patient Evaluation Letters	7	AN & Recovered AN	(29.5)	Out	Individual (FtF)	10	Once or twice weekly	Tchanturia & Davies in-house clinical protocol described elsewhere (see paper for details)	Initially confusing but mentally stimulating. Increased awareness of ones own thinking style. Both higher and lower levels of perfectionism post CRT.
Pretorius et al. (2012) <sup>5</sup>	Evaluation of group CRT for adolescents with AN through self-reported flexibility and motivation.	CFS, Motivational Ruler, Satisfaction Questionnaire	30 (1 male)	AN & EDNOS	12-17 (15.6)	Out	Group (FtF)	4	Once weekly	Tasks adapted from Genders & Tchanturia (2010)	No significant changes in flexibility and motivation to get better. Patient feedback: "interesting", "fun", "not too demanding", "helpful", but also "dull" and "repetitive". Patients wanted more variation in exercises.
Pretorius & Tchanturia (2007) <sup>1</sup>	To demonstrate how CRT has been adapted for AN through a case-report	Patient Feedback Letters, BMI	1	AN	31	In	Individual (FtF)	10	Twice weekly	Tasks focusing on flexibility and holistic thinking	Increase in BMI, enjoyed CRT, tasks were a bit repetitive but the patient developed new flexible strategies for implementation in real-life settings.
Tchanturia et al. (2008) <sup>3</sup>	To explore neuropsychological task performance before and after CRT.	MOCI, HADS, BMI, RCFT	27	AN	(28.8)	In	Individual (FtF)	10	Twice weekly	See details in paper	Improvements in cognitive performance on the Brixton & CatBat tasks. No significant improvements in other neuropsychological tasks were found. Significant decrease in depression was found.
Tchanturia et al. (2007) <sup>5</sup>	Explore the effect of CRT in set-shifting and investigates in acceptability for AN patients	MOCI, HADS, Cat Bat Task, TMT, The Brixton Test, the Haptic Illusion Task	4	AN	21-42	In	Individual (FtF)	10	--	The flexibility module developed for schizophrenia by Delahunty & Morrice (1993)	Improved cognitive flexibility and positive feedback for CRT.
Tchanturia et al. (2013) <sup>4</sup>	To describe current evidence and future research directions in CRT	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	CRT is an intervention worth researching.
Tchanturia et al. (2006) <sup>1</sup>	To demonstrate the potential benefits of CRT through a case-report	BMI, MOCI, HADS, TMT, the Brixton Test, Cat Bat, the Urzadze Illusion Task	1	AN	42	In	Individual (FtF)	10	Once or twice weekly	A cognitive remediation workbook focusing on flexibility	The authors propose cognitive flexibility training as a pre-treatment intervention for treatment resistant inpatient cases.

**Table 2. Continued**

Author (date)	Aim of Study	Outcome Measures	Sample Size	Patient Diagnosis	Sample Age/Range (Mean)	Setting	Mode of Delivery	Session Details	Intensity	Intervention Materials	Outcomes
Whitney et al. (2008) <sup>2</sup>	To examine patients' experience in participating in CRT.	Patient Feedback Letters	21	AN	17-54 (30.3)	In	Individual (FIF)	10	Once or twice weekly	A manual consisting of tasks focusing on flexibility and central coherence	Patients felt positive towards the fact that the intervention did not focus on food. It was helpful in reducing perfectionism and rigidity. More difficulty in tasks wanted, and help to implement newly learned skills.
Wood et al. (2011) <sup>2</sup>	To describe group CRT for adolescents	Patient Feedback and Clinical Impressions	9 (1 male)	AN	13-19	In	Group (FIF)	10	Once & twice weekly	A CRT manual for AN developed by Tchanturia et al. (2010)	Patients found CRT fun and playful, and CRT helped develop a positive therapeutic relationship. Negative feedback involved tasks being boring, too easy and repetitive. Some negative group dynamics affected the group work.
Zuchova et al. (2013) <sup>2</sup>	To explore the feasibility and acceptability of group CRT for inpatients with AN	Patient Feedback	34 (1 male)	AN	18-45	In	Group (FIF)	10	Once a week	Cognitive Remediation Flexibility Module for AN (details in paper)	Group-based CRT could be well incorporated into the therapeutic program of the Eating Disorders Unit. The intervention was well received by the participants

<sup>1</sup> = Single Case Studies; <sup>2</sup> = Feasibility Studies; <sup>3</sup> = Pre and Post CRT Assessment Studies; Without Control Groups; <sup>4</sup> = Theoretical/Empirical Papers; <sup>5</sup> = Additive/Combined Studies; <sup>6</sup> = RCT's Non Specific; Abbreviations: CRT = Cognitive Remediation Therapy; N.A. = Non Applicable; BMI = Body Mass Index; FIF = Face to Face; RCT = Randomized Controlled Trial  
<sup>\*</sup> = Interventions details (i.e. sample size and age, session details, intensity and intervention materials) refer to the CRT condition only.  
Abbreviations of patient diagnosis: AN = Anorexia Nervosa, EDNOS = Eating Disorder Not Otherwise Specified  
Abbreviations of outcome measures: EDE = Eating Disorder Examination; EDE-Q = Eating Disorder Examination Questionnaire; EDI-2 = Eating Disorder Inventory-2; EAT-26 = Eating Attitudes Test-26; EDRQ = Eating Disorders Belief Questionnaire; BDI = Beck's Depression Inventory; CY-BOCS = Children's Yale-Brown Obsessive-Compulsive Scale; MOCI = Maudsley Obsessive-Compulsive Inventory; HADS = Hospital Anxiety and Depression Scale; RSES = Rosenberg Self-Esteem Scale; STAI = State Trait Anxiety Scale; D-KEFS = Delis Kaplan Executive Function System; BRIEF-SR = Behavior Rating of Executive Function – Self Report; BRIEF-PF = Behavior Rating Inventory of Executive Function- Parent Form; RCFT = Rey Complex Figure Test; TMT = Trail Making Test; WCST = Wisconsin Card Sorting Test; IGIT = Iowa Gambling Task; CFS = The Cognitive Flexibility Scale; HSC = Hayling Sentence Completion Task; WAIS-III = Wechsler Adult Intelligence Scale, 3<sup>rd</sup> Edition; GAF = Global Assessment of Functioning Scale; TCI = Temperament and Character Inventory; CHQ = Child Health Questionnaire; FMDPS = Frost's Multi-Dimensional Perfectionism Scale; TSPE = Therapy Suitability and Patient Expectancy; HRQ = Helping Relationship Questionnaire

## **RESEARCH OBJECTIVES**

The principal aim of this doctoral thesis was to establish the feasibility of cognitive remediation therapy for adolescents with AN. Feasibility was explored in relation to:

- a) treatment delivery
- b) patient recruitment and retention
- c) assessment methods and materials

## METHODS & MATERIALS

### Study Design

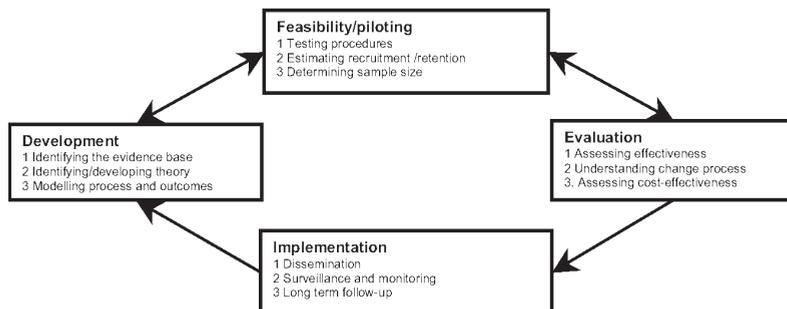
When evaluating complex interventions in mental health research, it is essential to conduct thorough early-phase piloting and developmental work. Generally, complex interventions contain several interacting components, and a good theoretical understanding of these components is essential in order to comprehend if, and how, the intervention might cause changes.

In 2010, we conducted the developmental phase in which we identified the various components of the intervention and the underlying mechanisms which are assumed to influence outcomes. Results from this initial phase was presented at the Eating Disorders Research Society 16<sup>th</sup> Annual Meeting (Lask et al., 2010) and at the 10th London International Eating Disorders Conference (Lask et al., 2011a, 2011b). When the present study was initiated in January 2011, there were still no reported formal studies of CRT for adolescents with AN, nor any detailed or structural templates to follow with regards to the development and evaluation of the intervention. Consequently we devised a programme for its evaluation, using the Medical Research Council (MRC) framework for developing and evaluating RCT's for complex interventions (Craig et al., 2008) (see **Figure 2**). A number of studies have previously described the practical application of this framework in health research (Hardeman et al., 2005; Murchie, Hannaford, Wyke, Nicolson, & Campbell, 2007; Pinnock et al., 2007; Richards et al., 2006), but this study is the first applying the model to an intervention targeting adolescent AN.

Using this framework for developing and evaluating CRT for adolescents with AN, the overall aim of this doctoral thesis was to establish a robust structure for a subsequent full-scale intervention. This was attempted by systematically planning, performing and evaluating step 1 and 2 in the feasibility/piloting phase, described as follows in the MRC framework:

*"The feasibility and piloting stage includes testing procedures for their acceptability, estimating the likely rates of recruitment and retention of subjects, and the calculation of appropriate sample sizes. Methodological research suggests that this vital preparatory work is often skimped. Evaluations are often undermined by problems of acceptability, compliance, delivery of the intervention, recruitment and retention, smaller-than*

expected effect sizes, and so on, that could be anticipated by thorough piloting. A pilot study need not be a ‘scale model’ of the planned main stage evaluation, but should address the main uncertainties that have been identified in the development work. Pilot study results should be interpreted cautiously when making assumptions about the required sample size, likely response rates, etc., when the evaluation is scaled up. Effects may be smaller or more variable and response rates lower when the intervention is rolled out across a wider range of settings. A mixture of qualitative and quantitative methods is likely to be needed, for example to understand barriers to participation and to estimate response rates. Depending on the results, a series of studies may be required to progressively refine the design, before embarking on a full-scale evaluation. (Craig, et al., 2008, p. 10)”.



**Figure 2.** The Medical Research Council (MRC) framework for developing and evaluating randomized controlled trials for complex interventions.

When testing the procedures of a novel intervention, several aspects have to be taken into consideration. Firstly, for which *elements* of the procedure do we aim to establish feasibility, and secondly, for *whom* do we wish to assess the feasibility of the intervention? The investigation of these aspects will guide the decision on whether it is appropriate to proceed with a full-scale evaluation (i.e. a RCT), or whether a series of additional studies are required in order to refine its design. As for aspects related to testing procedures, we chose to focus on *treatment delivery*, the *materials* used, and feasibility for *patients* (participants) and *clinicians* involved in the study.

As the aim of a feasibility/piloting study is to produce a replicable protocol than can be applied in the assessment of the effectiveness of the intervention, it was also imperative to investigate *how* to best assess potential change. Materials and methods selected to investigate such changes are described in more detail on page 43 Further, as a properly powered, and representative sample is a prerequisite to be able to establish the true effect of an intervention and the generalizability of results, aspects related to recruitment and retention were a pivotal part of this RCT-preparatory phase.

## **Project Management**

The study was conducted at the Regional Department for Eating Disorders (RASP) at Oslo University Hospital, Ullevål, HF. RASP is a highly specialized eating disorder clinic offering both in- and outpatient treatment for individuals with eating disorders. All necessary ethical procedures were followed; the project was registered at OUS, Ullevål HF (project no. 1506), the data protection service (Personvernombudet, Ullevål) approved the project, and the Regional Committees for Medical and Health Research Ethics (REK; ref 2010/1265a) granted us ethical approval. Informed consent was sought from all participants as well as from their parents when below the age of 16.

Three staff members at RASP were involved in the practicalities of conducting the study. The PhD candidate was responsible for the recruitment of patients, all CRT delivery (approximately 200 clinical sessions each lasting 45 minutes), and tasks related to the practicalities of administering, scoring and analysing pre- and post psychological assessment (i.e. self-report measures). A fellow PhD candidate and a research assistant aided in the process of conducting the neuropsychological assessment prior and post CRT (approximately 45 hours of face-to-face assessments). The PhD candidate was further responsible for developing and evaluating new materials suitable for working with young patients with AN (e.g. Lindvall, et al., 2010), dealing with administrative tasks related to the project such as self-report questionnaire- and neuropsychological test scoring, data entry, data analyses, and dissemination of results and feedback to patients and health care takers.

## **The Intervention – Cognitive Remediation Therapy**

All CRT sessions were delivered face-to-face, but in contrast to the original CRT in-house manual developed by Kate Tchanturia and colleagues at the Institute of Psychiatry, King's College London (Tchanturia & Davies, 2010), our CRT sessions were individually tailored to meet each patient's specific needs, rather than based on a pre-set number of sessions with a predetermined content. In accordance with previous CRT studies, no efforts were made to discuss or explore emotionally relevant themes such as food, weight or calories. Inevitably, some patients raised such issues but these were explored within the context of the patient's cognitive style, rather than through its psychological manifestations. Each session comprised a combination of practical tasks and reflections where the essence was to explore the

strategies used to tackle the tasks, considering possible alternatives and reflecting on the pros and cons of the strategies used. Thus it was not whether the task was successfully completed that mattered most, but how it was attempted. In essence, the patient was presented with a set of different tasks or games, and was asked to follow the therapist’s instructions in going about solving them. If the patient experiences difficulties in solving these, the therapist and patient together tried to figure out why the task was difficult to solve, how it might be solved in a different or more efficient way, what the pros and cons of the different strategies for the tasks were, and for everyday functioning. Most commonly, 1-2 tasks were administered each session. Tasks designed to enhance set shifting and central coherence were simple, easy to understand, and delivered in a playful way. The selection of tasks was based on the therapist’s clinical judgement, and chosen to address the particular cognitive style or difficulties specific to each patient. The meta-cognitive component, i.e. thinking about one’s own thinking process, designed to help patients explore their cognitive styles, was encouraged throughout the entire treatment process. To help the patient engage in the meta-cognitive process, all tasks were accompanied and followed by questions encouraging reflecting on one’s own thinking. Small variations of a predetermined set of questions were used throughout the CRT programme, allowing for fruitful reflections and discussion. A few of the most commonly used questions are shown in the table below (Table 3).

<b>Table 3. Guiding Questions in Cognitive Remediation Therapy</b>
<p><b>1. What did you think of this task/puzzle/game?</b></p> <ul style="list-style-type: none"> <li>• Was it easy or difficult?</li> <li>• In what way was it easy/difficult?</li> <li>• Did you like it/dislike it?</li> </ul> <p><b>2. How did you go about trying to solve it?</b></p> <ul style="list-style-type: none"> <li>• Did you use any particular strategy/technique/trick?</li> <li>• How did that particular strategy/technique/trick work for you?</li> <li>• Could you have completed it in a different way?</li> <li>• What would have been different if you had chosen a different strategy/technique/trick?</li> <li>• If you had been given the same task again, how would you have tackled it?</li> </ul> <p><b>3. Did you learn anything about your own thinking style while tackling the task/puzzle/game?</b></p> <ul style="list-style-type: none"> <li>• If yes, what did you learn</li> </ul> <p><b>4. Would you say that this particular thinking style is one that you use in other areas of your life as well (outside therapy sessions)?</b></p> <ul style="list-style-type: none"> <li>• Can you give me an example of an event or a situation where you might use the same “thinking style” or the same strategy/technique/trick in your day-to-day life?</li> <li>• What usually happens when you use that strategies/technique/trick in your daily life?</li> <li>• Could you approach challenges/tasks/chores differently in your daily life?</li> <li>• What do you think would happen if you did?</li> <li>• What do you think are the pros and cons of each strategy/trick?</li> </ul>

### *Session Focus*

Clinicians can adopt various approaches when deciding upon which domain(s) to focus. The first approach, which for many might appear as the most logical, is to select tasks and puzzles on the basis of neuropsychological test results. By doing so, the CRT exercise program will be individually tailored and addressing the core features of the patient's cognitive style. However, clinicians might experience patients to be, for example, extremely rigid although scoring in the normal range on tests assessing flexibility and set-shifting. Thus, another approach is to assess neurocognitive abilities clinically during the course of CRT. We chose to adopt the latter approach as there were few studies exploring neuropsychological functioning in young patients with AN when this study was initiated, and the clinical implications of performance based weaknesses that CRT targets, were relatively unknown for this patient group.

### *Homework*

An important part of CRT is to explore how the knowledge acquired in therapy can be transferred to real life settings. To be able to do this, small homework tasks were introduced once the patient seemed ready. The aim of these tasks was for the patient to use the knowledge acquired during CRT sessions, and to experiment with this knowledge outside the therapy context. The tasks were fairly simple and related to everyday routines, which were easy to alter and reflect upon. Similar to the tasks presented during CRT, the exercises were not supposed to elicit strong emotional reactions, and were usually not related to explicit features of the illness (e.g. food, calories, weight, body). The choice of homework tasks was always guided by the therapist's impression of specific issues needing to be addressed, and the patient's interest or willingness to try to change these. By ensuring a collaborative process when choosing homework, the patient was encouraged to reflect on issues of personal interest, and to take ownership of her process of change. Initial homework tasks were usually neutral (i.e. not individual specific), but as the course of CRT progressed, more specific homework tasks guided by individual preferences were designed for each patient. A few examples of initial (neutral) homework tasks are listed in **Table 4**.

**Table 4. Examples of CRT Homework Tasks**

- When you get dressed, put on your clothes in a different order than you usually do
- Try describing the route from home to school/work/the store/your favourite café to someone else
- Choose another route when coming to your next CRT session
- Leave your bed unmade an entire day
- Watch a movie at home, and summarize the plot to your CRT therapist next time you meet
- Collect leaves/flowers/shells/pictures to make a collage
- Try describing yourself by first writing a short text about yourself, then shorten it down to a few sentences, and finally, summarize the text in just a few words
- Use the letters in the alphabet, one by one, to describe yourself
- The next time you go to your favourite café, try choosing another type of coffee/tea
- Wear your wristwatch on the other arm for one day
- Think of something that irritates you and make a plan for doing something about it
- Describe your family members, one by one using no more than 3 words per person. What are their good/less good sides?

*Cognitive Remediation Therapy for Children and Adolescents with Anorexia Nervosa: The CRT Resource Pack*

Given CRT was originally developed for adults and tends to use adult-oriented materials (Tchanturia & Davies, 2010; Tchanturia, et al., 2010), it became necessary for us to develop more age-appropriate materials for the adolescents taking part in our study. The adaptation of adult CRT materials involved developing, testing and evaluating exercises, tasks, games and puzzles selected specifically for use with young patients. The tasks chosen were informed by their means of age appropriateness, the domains they targeted, and the difficulty levels through which they could be administered. Since we wished for the intervention to have a strong focus on making the sessions fun and enjoyable, the games that were developed and sourced were appealing and fun, colourful and challenging with a variety of levels of difficulty (Owen, Lindvall Dahlgren, & Lask, 2013). Tasks were a combination of pen and paper tasks (some of which were adapted from the original CRT manual, others developed by the PhD candidate and colleagues), and various games purchased from the online web store [www.thinkfun.com](http://www.thinkfun.com). Also, with the permission from Pedverket Kompetanse, a few tasks focusing on set-shifting and flexibility developed by Gunvor Sønnesyn (Sønnesyn, 2010, November 11) were also used during the CRT sessions. A collection of the tasks and exercises sourced and developed were collected in the CRT Resource Pack (Lindvall, et al., 2010), and were made available free of charge at the RASP website ([www.rasp.no](http://www.rasp.no)). An overview of the tasks in the CRT Resource Pack, and the domains they target can be found in Appendix I, in which tasks are listed in order of appearance in the CRT Resource Pack. As evident from the table, domains are not mutually exclusive, but rather overlapping in nature. Tasks used during CRT can therefore be understood as training multiple functions

simultaneously. A few of the tasks listed at the bottom of the table are not to be found in the CRT Resource Pack, but were developed or purchased after it had been published online in 2011. These tasks are marked with an asterisk (\*).

### **Treatment Fidelity**

The PhD candidate, holding a M.A. degree in social psychology from the University of Oslo, was trained in CRT by a fellow psychologist at Oslo University Hospital who had previously attended a CRT for AN workshop on, held by one of the developers of CRT (Dr. Kate Tchanturia). The PhD candidate administered all CRT sessions. During the data collection period, lasting approximately 18 months, weekly supervision meetings were held where CRT delivery, case specifics and general CRT issues were discussed. These meetings were initially moderated by Professor Bryan Lask, and later, by Dr. Øyvind Rø, and followed by fellow psychologists and psychiatrists at the Regional Department for Eating Disorders (RASP) at Oslo University Hospital, competent in the field of CRT (Garte, Graver, Øverås, Frampton, & Isdahl, 2010).

The study protocol was inspired by the CRT work of Dr. Kate Tchanturia at the Institute of Psychiatry, King's College in London, resting on clinical observations and well documented research evidence of weaknesses in set-shifting and central coherence in adult patients with AN. However, our protocol was modified to suit young individuals, and the intervention was tailored to address the specific needs of each patient in terms of developmental status and cognitive styles. The CRT Resource Pack was used throughout the course of the intervention, and with minor variation, patients were encouraged to tackle the same set of tasks and games, after which thinking strategies were reflected upon and challenged. Systematic recordings were made after each CRT session, which were available to the patients' treatment team through the electronic patient record system. These recordings included the following:

- 1) the specific task(s) used during the session
- 2) how the patient tackled the task(s)
- 3) the patient's ability to reflect on the strategies used to tackle the task(s)
- 4) an overall evaluation of the session based on the CRT therapist's clinical impression
- 5) homework assignments and how the patient tackled these

Alongside being responsible for delivering CRT to the participants in the study, the PhD candidate was involved in organising national and international CRT courses and workshops for health care professionals wishing to learn more about the adaptation of CRT for young patients with AN, and the practicalities of its delivery and assessment. Examples of these are three two-day courses at Regent's College in London, UK, organised and led by the PhD candidate together with Professor Bryan Lask. Also, the PhD candidate tutored colleagues at the Stockholm Center for Eating Disorders in Sweden, and regularly organised workshops both nationally and internationally on CRT for young patients with AN. As part of the development of CRT for young patients with AN, an annual, international CRT network meeting was initiated by the PhD candidate in 2010. The aim of the network meeting was to stimulate knowledge sharing, and to bring together clinical and research oriented work in this field. The first meeting was hosted by Professor Bryan Lask at Ellern Mede Clinic, London; a specialist hospital providing intensive care for young patients with eating disorders. Following this initial meeting, meetings have been organised annually, with the PhD candidate being responsible for recruiting new members, updating members regarding new research in the field and keeping an overview of the field as a whole.

### **Recruitment and Data Collection**

The two recruiting centres, the Regional Department for Eating Disorders (RASP) and Barnesenteret (the Paediatric Unit) at Oslo University Hospital, Ullevål HF, have a good track record of cooperating in recruiting patients to various research projects at RASP. The recruitment of patients to the study was a well-organised, collaborative process including the PhD candidate and clinicians at the two units. As for patients recruited from the inpatient unit (RASP), the PhD candidate was updated weekly regarding new admissions. To approach new patients and parents with the aim of informing them about the project, approval had to be sought and granted from the clinician(s) responsible for each individual patient. At the outpatient unit (the Paediatric Unit), one clinician updated the PhD candidate via email or telephone about potential participants, which were then contacted via telephone, and invited to an informal information meeting at RASP. All parents had approved their child's participation in the study.

Prior to the commencement of CRT, patients were assessed using measures described in the Materials section. Participants then received between 7 and 12, once or twice weekly

individually delivered sessions, after which they were re-tested using the same measures as before the intervention. In addition, patients were asked to fill out a treatment evaluation questionnaire post CRT, allowing us to explore the acceptability of the treatment for this particular patient group.

## **Participants**

As this study was exploratory in assessing the feasibility of CRT for adolescents with AN, rather than designed to measure potential change as a direct result of the intervention, the size of the sample was not crucial in this particular phase. Further, there were no previous studies exploring feasibility of CRT for adolescents, making sample size estimation based on well-documented criteria challenging. Our sample size was therefore based on an estimation of how many patients we thought we would be able to recruit during the course of the 2-year recruitment process, and corresponded to the number of patients admitted to both units fulfilling the inclusion criteria during this particular time span (i.e. a convenience sample).

The prevalence of AN is at least ten times higher in females than males, and the vast majority of patients admitted to RASP and Barnesenteret are female. To ensure a representative sample, we choose to recruit females only. 24 patients (13 inpatients and 11 outpatients) were informed about the study, and given the opportunity to participate. Two inpatients declined due to the fact that they both would be discharged soon after the initial information meeting. Another inpatient first accepted the invitation to participate in the study, but withdrew before having initiated the first session. Her reason for withdrawing was that she was too occupied with schoolwork and treatment sessions at the ward. One outpatient and her parents participated in the introductory meeting, but decided not to take part in the study after having discussed potential implications of participation. This girl was at the time in a process of efficiently increasing her weight, and was functioning satisfactorily in her everyday life. Her parents were concerned about their daughter's potential relapse by bringing the eating disorder back into focus (as in a therapeutic setting), and especially, when in contact with other girls with eating disorders at the ward.

A total of twenty inpatients (N=10) and outpatients (N=10) aged 13-18, (mean = 15.9, SD = 1.6) agreed to participate in the study. Descriptive data dividing the sample into in- and outpatients are presented in **Table 5**.

**Table 5. Descriptive data for in- and outpatients at T1**

	Outpatients (N=10)			Inpatients (N =10)			
	N	Mean (SD)	Range	N	Mean (SD)	Range	
Age (years)	10	15.76 (1.77)	13.10-18.66	10	16.03 (1.56)	13.95-18.51	
BMI Percentile	10	11.14 (9.20)	0.00-28.01	10	9.35 (23.18)	0.05-75.05	
Performance IQ <sup>1</sup>	WASI-III	7	12.71 (2.98)	9.00-16.00	8	10.25 (2.12)	7.00-14.00
	WASI	3	56.67 (7.02)	50.00-64.00	2	53.00 (7.07)	48.00-58.00
Verbal IQ <sup>2</sup>	WASI-III	5	10.80 (.45)	10.00-11.00	4	9.00 (1.63)	7.00-11.00
	WISC-III	5	11.00 (1.87)	9.00-13.00	6	8.17 (3.31)	2.00-12.00

SD = Standard Deviation. <sup>1</sup>=Matrix Reasoning Subtest from the Wechsler Adult Intelligence Scale 3<sup>rd</sup> Edition (WAIS-III) and Wechsler Abbreviated Intelligence Scale 3<sup>rd</sup> Edition (WASI-III), <sup>2</sup>= Vocabulary Subtest from WAIS-III and Wechsler Intelligence Scale for Children 3<sup>rd</sup> Edition (WISC-III)

Weight and height was measured shortly prior to (T1), and after (T2) the intervention. Hospital medical records revealed that patients were severely underweight when first admitted (T0) to the two units (Mean BMI percentile = 1.6, *SD* = 3.1). At the time of recruitment (T1), weight had increased significantly [ $t(19) = 2.41, p = .026$ ], and the mean BMI percentile was just above 10% (Mean = 10.2, *SD* = 17.2). There were no significant differences between in- and outpatients in BMI percentiles at T1. Based on self-reports of binge eating and compensatory behaviours, 18 patients were classified as having a restricting subtype of AN (AN-R). The two remaining patients fitted the description for a binge-purge subtype (AN-BP). Between T0 and T1, one inpatient had reduced underweight markedly, and during this time span, increased her BMI percentile from a pathologic level of 5.4 at admission, to a healthy BMI percentile of 75 at the initiation of the intervention (CRT). When this participant was removed from the analysis, a new mean T1 BMI percentile score of 6.8 (*SD* = 8.1) emerged for the 19 remaining participants.

Data from all 20 patients were included in Paper I, whereas the number of participants included in the data analyses in Paper II and III (ranging from 16 to 20) was dependent on complete assessments being made both before and after CRT. In addition to patient data, data from 16 parents were included in paper III. This data represents parental ratings of their child's executive functioning, and only complete assessments (i.e. full data sets from *both* patients and parents before and after CRT) were included in the statistical analyses in this paper.

## Assessment Materials

This section describes the assessment materials in more detail, starting with the test battery used to assess neuropsychological functioning in Paper II – the Ravello Profile (Rose, et al., 2011).

### *The Ravello Profile*

We used a standardized test battery called “the Ravello Profile” (Rose, et al., 2011) (see **Table 6**) to assess neuropsychological functioning in our sample. The Ravello Profile includes a variety of test with well-established psychometric properties (Stedal, et al., 2012), chosen on the basis of previous studies reporting consistent weaknesses in cognitive flexibility and central coherence in females with AN (Lopez, Tchanturia, Stahl, Booth, et al., 2008; Lopez, Tchanturia, Stahl, & Treasure, 2008; Roberts, et al., 2007).

**Table 6. The Ravello Profile Neuropsychological Assessment Battery (Rose, et al., 2011)**

Domain & Subdomain	Task	Assessment Material
IQ		
Performance IQ	Matrix Reasoning	WAIS-III / WASI
Verbal IQ	Vocabulary	WAIS-III / WISC-III
Executive Functioning		
Cognitive Inhibition	Colour Word Interference Condition 3	D-KEFS
Cognitive Inhibition & Flexibility	Colour Word Interference Condition 4	D-KEFS
Verbal Fluency	Verbal Fluency Condition 1	D-KEFS
Verbal Fluency	Verbal Fluency Condition 2	D-KEFS
Switching	Verbal Fluency Condition 3	D-KEFS
Switching	Trail Making Test Condition 4	D-KEFS
Planning & Inhibition	Tower of London	D-KEFS
Flexibility & Spatial Working Memory	Brixton Spatial Anticipation Test	Hayling & Brixton
Visio-Spatial Memory	Immediate Recall	RCFT
	Delayed Recall	RCFT
Visual Spatial Processing	RCFT Style Index	RCFT
	RCFT Order of Construction Index	RCFT
	RCFT Central Coherence Index	RCFT
	Group Embedded Figures Test	GEFT*

*Note.* WAIS-III = Wechsler Adult Intelligence Scale (Wechsler, 1997); WASI = Wechsler Abbreviated Scale of Intelligence (Wechsler, 1999); WISC III = Wechsler Intelligence Scale for Children (Wechsler, 1992); D-KEFS = Delis Kaplan Executive Function System (Delis, Kaplan, & Kramer, 2001); Hayling & Brixton (Burgess & Shallice, 1997); RCFT = Rey Complex Figure Test (Delis, et al., 2001; Lopez, Tchanturia, Stahl, Booth, et al., 2008); \* = Not part of the Ravello Profile. GEFT = Group Embedded Figures Test (Witkin, Oltman, Raskin, & Karp, 1971).

The test battery is designed for usage with individuals between the ages of 6-89, and includes the following subtest from the Delis Kaplan Executive Functioning System (D-KEFS) (Delis, et al., 2001): The Verbal Fluency Test (VFT), the Trail Making Test (TMT), the Color Word Interference Test (CWIT) and the Tower of London (ToL). Also included is the Rey Complex

Figure Test (RCFT) developed by Osterrieth (Osterrieth, 1944), the Brixton Test (Burgess & Shallice, 1997) and the Group Embedded Figures Test (GEFT) (Witkin, et al., 1971). The GEFT is not a test included in the Ravello Profile, but was included as it produces measures of detailed vs. global information processing. As an indication of general verbal abilities, the Vocabulary subtest from the Wechsler Adult Intelligence Scale – Third Edition (WAIS-III) (Wechsler, 1997), and the Wechsler Intelligence Scale for Children – Third Edition (WISC-III) (Wechsler, 1992) were used. Corresponding non-verbal (i.e. performance) skills were assessed using the Matrix Reasoning subtest from the WAIS-III and the Wechsler Abbreviated Scale of Intelligence (WASI) (Wechsler, 1999).

### *Psychiatric Assessment*

*EDE-Q.* Eating disorder psychopathology was assessed using the self-report version of the Eating Disorder Examination (EDE) (Fairburn & Beglin, 1994); the Eating Disorder Examination Questionnaire version 6.0 (EDE-Q 6.0) (Fairburn & Beglin, 2008). The EDE-Q is a 28-item self-report questionnaire, which focuses on eating disorder behaviours and attitudes during the previous 28 days. Responses on the 22 items addressing attitudinal aspects of the ED psychopathology are scored on a 7-point Likert scale (0-6), and generate subscale scores reflecting the severity of four different aspects of ED psychopathology; Dietary Restraint, Eating Concern, Weight Concern and Shape Concern. Together, the four subscales generate a Global Score thought to yield an overall measure of ED psychopathology. The EDE-Q has shown to have acceptable psychometric properties both in its original English form (Berg, Peterson, Frazier, & Crow, 2012; Mond, Hay, Rodgers, Owen, & Beumont, 2004) and when translated to Norwegian (Rø, Reas, & Lask, 2010).

*BDI-II.* Depression was assessed using Beck's Depression Inventory (BDI-II) (Beck, Steer, & Brown, 2005a) which is among the most widely used scales for self-ratings of depressive symptoms. It contains 21 items, with item scores ranging from 0-3, which are added to obtain a composite score. Standard cut-off scores are as follows: 0-9 = minimal depression, 10-18 = mild depression, 19-29 = moderate depression and 30-63 = severe depression. The inventory has proven to have high internal consistency in both psychiatric and non-psychiatric samples, and high content and convergent validity with other forms for depression rating scales (Beck, Steer, & Carbin, 1988; Richter, Werner, Heerlein, Kraus, & Sauer, 1998). We used a

validated Norwegian translation of the inventory to assess symptoms of depression in our sample (Beck, Steer, & Brown, 2005b).

STAI. The State Trait Anxiety Inventory (STAI) (Spielberger, Gorsuch, & Lushene, 1983) is a 40-item self-report questionnaire yielding subscale scores of state (i.e. temporary, right now, at this moment) and trait (i.e. across situations and time, generally) anxiety, and a composite score representing overall anxiety. The inventory is based on a 4-point Likert scale where the scale for state anxiety is “not at all” (1), “somewhat” (2), “moderately so” (3) and “very much so” (4). The 4 point scale for trait anxiety is as follows: “almost never” (1), “sometimes” (2), “often” (3) and “always” (4). Sum scores can be calculated separately for state and trait anxiety, and a total sum score indicates the overall level of anxiety on both scales. Overall sum scores range from 20-80 with higher scores indicating higher levels of severity. Clinical significance is normally determined by using a cut-off score around 40 (Forsberg & Björvell, 1993; Knight, Waal-Manning, & Spears, 1983). The two scales are thought to have high discriminant and convergent validity with other measures of anxiety, and internal consistency coefficients for the scale have ranged from .86 to .95 (Spielberger, et al., 1983). Over a 2-month interval, it has been possible to establish test-retest reliability with coefficients ranging from .65 to .75, and there is evidence of both construct and concurrent validity of the scale (Spielberger, 1989). The STAI has been translated into Norwegian by Håseth, Hagtvet and Spielberg (1990), with norms being established using Norwegian high school and college students (Håseth, Hagtvet, & Spielberger, 1993).

ChOCI. The Norwegian translation of the self-report instrument ChOCI (Children’s Obsessional Compulsive Inventory) (Øverås, Reas, & Frampton, Accessed January 2011) was used to assess OCD in our sample. The ChOCI is a self-report version of the Children’s Yale-Brown Obsessive Compulsive Scale (CY-BOCS) (Goodman, Rasmussen, & Price, 1986) and yields non ED-specific measures of obsessions and compulsions which are described in relation to five different aspects of the disorder 1) the level of everyday interference caused by the obsessions/compulsions, 2) the degree to which the child can resist the obsessions and/or compulsions, 3) the amount of time devoted to obsessions and/or compulsions, 4) the level of despair experienced by the child and 5) the perception of control over ones obsessions and/or compulsions. Scores are rated on a 5-point Likert type scale (0-4) with scores above 17 being considered as clinically significant (Shafran et al., 2003). The ChOCI has proven to have high levels of internal consistency for all four subscales ( $\alpha > 0.8$ ), strong inter-total correlations ( $r$

= 0.56-0.89,  $p > 0.01$ ) and satisfactory discriminant validity (Shafran, et al., 2003). Due to too much missing data, the ChOCI was not included in any of the analyses.

### *Executive Functions*

***BRIEF.*** The Behavior Rating Inventory of Executive Function (BRIEF) is a standardized questionnaire developed for children and adolescents between the ages of 11 and 18, and parents and teachers of school aged children between 5 and 18. It yields evidence of executive function behaviors in school and home environments, and can serve as an important adjunct to clinical evaluation and neuropsychological assessments of executive dysfunction. In our study, the Norwegian translation (Sørensen, Plessen, Nicholas, & Lundervold, 2011) of the self-report version (BRIEF-SR) and parent version (BRIEF-PF) were used to establish everyday executive functioning as assessed by the patients themselves, as well as their parents. Psychometric properties of the Norwegian version of the BRIEF have proved acceptable, and support the use of American norm data and the reliability of the clinical index scores (Fallmyr & Egeland, 2011).

The BRIEF-SR yields information about young people's views of their own executive functions in every day life settings. The questionnaire contains 80 items, and the informant is asked to reply to each item based on the following statement "Over the past 6 months, how often has each of the following behaviors been a *problem*?" Expressions such as "*I get upset by a change in plans*", "*I am impulsive*", "*I get caught up in details and miss the main idea*", "*I get upset over small events*" and "*I have trouble prioritizing my activities*" are scored on a 3-point Likert scale: "never", "sometimes", and "always," and provides scores on eight clinical scales describing various aspects of executive functioning. The four subscales, Inhibit, Shift, Emotional Control and Monitor, are combined to produce a broader index called the Behavior Regulation Index (BRI), and the remaining four subscales, Working Memory, Plan/Organize, Organization of Materials and Task Completion comprise the Metacognitive Index (MI). The overall score, the Global Executive Composite (GEC), is a composite of the two index scores.

The parent form of the BRIEF (BRIEF-PF) (Gioia, Isquith, Guy, & Kenworthy, 2000) is designed to be completed by the caregiver, and is an 86-item questionnaire designed to provide detailed knowledge of the child's behavior in every-day settings. Similar to the

BRIEF-SR, items such as *”Acts upset by change in plans”*, *”Has trouble waiting for turn”*, *”Says the same things over and over”* and *”Has trouble moving from one activity to another”* are rated based on the frequency with which the respondent experiences the child having problems with various behaviors related to executive functioning during the last six months. The BRIEF-PF overlaps with the BRIEF-SR on the following subscales: Inhibit, Shift, Emotional Control, Working Memory, Plan/Organize, Organization of Materials and Monitor. Adding a ninth subscale labelled “Initiation”, these clinical subscales together produce the same two indexes as the BRIEF-SR: the BRI and the MI, as well as a composite score (GEC). The eight overlapping clinical scales, as well as the ninth scale specific to the BRIEF-PF are described in more detail in **Table 7**.

Clinical Scale	Description and interpretations of scale
Inhibit	The ability to inhibit, resist, or not act on an impulse. Also refers to the ability to stop one’s own behavior at an appropriate time.
Shift	The context-dependent ability to move freely from one activity, situation or aspect of a problem to another. Includes making swift transitions, problem-solve flexibly and switch or alternate attention.
Emotional Control	The ability to adjust emotional responses in an appropriate and constructive way
Monitor	The ability of the child to assess its own performance to attain knowledge of progress in terms of personal goals and achievements. Also a personal monitoring functioning to ensure the effect on one’s own behaviors on others
Working Memory	The ability to hold information in mind with the purpose of completing a task or activity
Plan/Organize	The ability to tackle demands, both current and future-oriented. To be able to anticipate future demands, to set goals and to time-efficiently develop strategies for goal achievement
Organization of Materials	The orderliness of work, play and storage spaces (bedroom, lockers, desks etc.)
Task Completion <sup>1</sup>	The ability to finish or complete task appropriately and within a given timeframe
Initiate <sup>2</sup>	The ability to initiate a task or an activity. Independent generation of ideas, responses or strategies to solve problems

<sup>1</sup> = Only in the BRIEF-SR version; <sup>2</sup> = Only in the BRIEF-PF version

Both BRIEF-SR and BRIEF-PF are standardized assessment instruments with well-established psychometric properties (Guy, Isquith, & Gioia, 2004). For the BRIEF-SR, high internal consistency has been shown for the 80-item GEC (.96), and test-retest reliability is supported by correlations among clinical scales ranging from .59 to .85. Higher correlations were observed for the index scores BRI and MI (.84 and .87 respectively), with the highest correlation (.89) emerging for the GEC (Walker & D’Amato, 2006). Convergent evidence of validity is further supported by moderate correlations (for GEC,  $r = .56$ ) between BRIEF-SR and BRIEF-PF. For the BRIEF-PF, high internal consistency has been reported (.80 - .98),

and test-retest correlation ranging from .81 (clinical scales) to .88 (GEC) with the highest correlation emerging for the metacognitive index (MI) (.88) (Gioia, et al., 2000).

#### *User Feasibility – The CRT Treatment Evaluation Questionnaire*

A CRT treatment evaluation questionnaire was developed by the PhD candidate and colleagues in order to be able to explore user (i.e. patient) feasibility (see English translation in Appendix II). It is based on a combination of CRT specific items developed by Lindvall Dahlgren, Rø & Halvorsen (December 2010) (e.g. “*did you acquire any skills during the CRT sessions that might be useful in your everyday life?*”, “*how did you experience the division between practical exercises and discussion during the sessions?*” and “*how has the way you reflect on your own thinking changed during the course of CRT?*”) as well as items based on those developed by Kunnskapssenteret (Holmboe, Groven, & Olsen, 2008; Sjetne, Bjertnæs, & Iversen, 2009) (e.g. “*all in all, how satisfied or dissatisfied are you with the course of CRT you have received?*”, “*did you experience CRT being relevant to your situation?*”, “*how is your relationship to your family now, compared to before you started the CRT treatment program?*” and “*how are things working out in your everyday life now, compared to before you entered the CRT treatment program?*”) and RIKSÄT (Lago, Norring, & Engström, Accessed December 2010) (e.g. “*were you treated with respect during the course of CRT?*” and “*did your CRT therapist listen to you?*”).

The questionnaire contains 20 items which are divided into 4 sections, each exploring different aspects of the treatment: i) general assessment (i.e. general attitudes towards the treatment), ii) the treatment itself (i.e. detailed aspects of treatment delivery such as session length, number of sessions, materials etc.), iii) the perception of change in relation to the eating disorder and life in general after CRT, and iv) the relationship to the CRT-therapist. The treatment evaluation questionnaire is based on a five point Likert scale, with responses varying qualitatively depending on the characteristic of each question. E.g., the scale for responding to the question “*To what extent did you feel that the CRT sessions were useful to you?*” was “not at all useful”, “somewhat useful”, “quite useful”, “very useful” and “extremely useful”, whereas the scale options for responding to the question “*To what extent do you experience distress in relation to your eating disorder now, compared to before you started the CRT treatment program?*” were “a lot more than before”, “a little more than

before”, “it is more or less the same as before”, “a little less than before” and “a lot less than before”.

## Statistical Analyses

In this section, scoring procedures and details of the statistical methods used are outlined.

### *Scoring*

In this section, scoring procedures will be presented for measures used in paper I, II and III. All statistical analyses were carried out using PASW<sup>®</sup> Statistics 18 for Windows XP/Vista<sup>®</sup>.

*BMI and BMI Percentiles.* Both body mass index (BMI) and BMI percentiles were calculated shortly prior to, and post CRT. Whilst BMI is a measure of a persons weight for height ratio applying to adults (see **Figure 3**), BMI percentiles also takes into account age and gender, making it a more precise instrument for assessing weight in young, developing children and adolescents such as those included in our study. BMI percentiles of 10 % or less are comparable to the adult ICD-10 AN criteria of a BMI of 17.5 or lower (Hebebrand, et al., 1996).

$$\text{BMI} = \frac{\text{mass (kg)}}{(\text{height (m)})^2}$$

**Figure 3.** The BMI as a function of the individual’s body mass divided by the square of their height

*Psychiatric Assessment.* Measures of eating disorder psychopathology (EDE-Q), depression (BDI-II) and anxiety (STAI) are presented using raw scores, and are described in more detail in the Materials section. Scoring procedures for these tests are performed identically in paper II and III.

*Neuropsychological Scorings.* RCFT test performance was scored using Meyers & Meyers (Meyers & Meyers, 1995) measures of visio-spatial memory, and the Lopez et al. (Lopez, Tchanturia, Stahl, Booth, et al., 2008) scoring method of visio-spatial constructional abilities, which yields three different indexes. The *Style Index* (SI) indicates the extent to which the drawing process is characterized by continuity or fragmentation, and is scored using six pre-

selected items which are given a score between 0 and 2 (higher scores indicating a more coherent drawing process). The sum score is then divided by six yielding a Style Index score ranging from 0 to 2. The *Order of Construction Index* (OCI) indicates the preference of global external and/or local perimeter elements in the copying process, and is based on the first six complete elements drawn by the participant. Each of these six elements is given a score from 0 to 4, higher scores indicating higher importance with regards to the overall gestalt. The sum of these six elements are divided by six, yielding the OCI index score which ranges from 0 to 3.3. Finally, the *Central Coherence Index* (CCI) is calculated using the equation presented in **Figure 4**, and is thought to reflect an overall measure of central coherence.

$$CCI = \frac{OCI}{3.3} + \frac{SI}{2}$$

**Figure 4.** Central Coherence Index (CCI) Equation

For the greater part of the neuropsychological tests, raw scores were converted to scaled scores using Scandinavian age-based test norms. Exceptions were the Brixton Spatial Anticipation Test and the Group Embedded Figures Test (GEFT) for which norms for children and adolescents are not available. For the purpose of performing regression analyses, all neuropsychological test scores were converted from scaled scores to Z-scores using the equation presented in **Figure 5**. Z-scores have a mean of zero and a standard deviation of 1. The Z score indicates the number of standard deviations the converted test score is above, or below, the mean. For the Brixton Spatial Anticipation Test, recently published control group means from a child and adolescent sample were used (N =66) (Stedal, et al., 2012). In absence of child and adolescent GEFT norms, normative data from a sample of female college students (N=242) were used (Witkin, et al., 1971).

$$Z = \frac{X - M_x}{\sigma_x}$$

**Figure 5.** Conversion of scaled scores to Z-scores

**BRIEF Scorings.** The self-report version (BRIEF-SR) and parent version (BRIEF-PF) are scored similarly, but the former has 80 items, and the latter 86. As mentioned in the Materials section, items are scored on a 3-point Likert scale: “never”(1), “sometimes”(2), and “always”(3), and provide scores on eight clinical scales describing various aspects of executive functioning. Scaled BRIEF-SR scores are transformed to age and gender corrected

t-scores ( $M=50$ ,  $SD=10$ ), for which higher scores indicate higher degrees of executive dysfunction. T-scores at or above 65 (i.e. 1,5  $SD$  above the normative mean) are considered clinically significant in terms of executive dysfunction. As with the BRIEF-SR, BRIEF-PF scores are also transformed to age and gender corrected T-scores (based on the child's age and gender), where higher scores indicate higher degree of impairment, and T-scores at or above 65 are considered clinically significant.

### *Significance Testing and Effect Size Calculation*

Whereas significance tests tell us whether an effect is present in a given population, effect sizes are measures of the degree to which these effects are present, i.e., how strong or weak those effects are. Since the primary purpose of research designed to evaluate interventions is to investigate whether changes (i.e. the presence of effects) occur during the course of the intervention, and to estimate the magnitude and direction of these effects (i.e. the practical significance of the results), both t-tests generating information regarding the statistical significance of our results, and effect size calculations estimating the magnitude of changes observed were performed. Our preliminary analyses ensured normal distribution in both neuropsychological test scores (Paper I) and self-reported executive functioning (Paper II) indicating the use of a two-tailed (nondirectional) paired sample *t*-test.

There are numerous ways of calculating effect sizes. To achieve our aim of evaluating within-group effect sizes of test score means pre and post CRT, we chose to calculate *Cohen's d* (Cohen, 1988) using the equation displayed in **Figure 6**. The equation illustrates the function of *d* being the mean difference of tests scores [i.e. before and after CRT ( $M_1 - M_2$ )] over the pooled standard deviation [i.e. the common population standard deviation ( $SD_{pooled}$ )].

$$Cohen's\ d = \frac{M_1 - M_2}{SD_{pooled}}$$

**Figure 6.** The calculation of *Cohen's d*

*Cohen's d* effect sizes are labelled “small” ( $d = .2$ ), “medium” ( $d = .5$ ) or “large” ( $d = .8$ ), and indicate the size of the effect in terms of standard deviation units (Ellis, 2010a). The larger the *Cohen's d* is, the larger the effect. When calculating effect sizes using data from repeated measures within-group (i.e. dependent groups) studies (as the case in our study), it is useful to

correct for dependence among means, as the effect size is not only a function of the relation between changes in means and standard deviations, but also a function of the pretest-posttest correlations. To calculate effect sizes in accordance with the design of our study, we used an effect size calculator (Depeda, Accessed Jan-Dec 2013) applying Morris and DeShon's (2002) *Equation 8* (see **Figure 7**). This equation takes account for pre- and post test correlations where  $\delta_{RM}$  (i.e. the effect size using repeated measures) is explained as a function of the expected mean difference between scores at the two points of measurement ( $\mu_D$ ) divided by the standard deviation of the mean difference between pre and post test scores ( $\sigma\sqrt{2(1-p)}$ ).

$$\delta_{RM} = \frac{\mu_D}{\sigma\sqrt{2(1-p)}} = \frac{\delta_{IG}}{\sqrt{2(1-p)}}$$

**Figure 7.** Morris and DeShon's *Equation 8*

### *The Bonferroni Correction – An Ad-Hoc Method to Adjust for Multiple Comparisons*

When performing multiple statistical tests, there is always a risk that a fraction of these will be false positives, i.e. that one will make a Type I error (rejecting the null hypothesis) when the null hypothesis is actually true. The risk of making a Type I error increases with the number of comparisons made. For example, if doing 100 statistical tests for which the null hypothesis is true, it would be expected that 5% (corresponding to an  $\alpha$ -level of .05) of these (i.e. 5 tests) would be significant merely due to chance. In other words, five out of a hundred test results would represent false positives. If doing 200 statistical tests, the potential number of false positives would rise to 10, and so on. Adjustments for multiple comparisons is a statistical principle thought to alleviate some of the problems associated with this phenomenon, and an “insurance policy” against rejecting the null hypothesis by mistake (Rothman, 1990).

There are numerous ways in which researchers can remedy the risks associated with multiple comparisons, and many of these typically involve adjusting the  $\alpha$ -level. Some researchers simply tighten the alpha level to a more strict value of .001, whereas others adopt one of the most commonly methods used; the *Bonferroni* correction. The Bonferroni correction is an ad-hoc method and can be described as  $\alpha/N$ . In this equation,  $\alpha$  represents the significant test

level that one would have applied had one tested merely one hypothesis.  $N$ , on the other hand, represents the number of tests being run on the same data set.

There is no general consensus of when, or if one should actually correct for multiple comparisons, and the statistical literature is characterized by contradictory arguments stating both pros and cons of this method. In reality, although decreasing the risk of making a Type I error, tightening the  $\alpha$ -level simultaneously increases the risk of making a Type II error (failing to reject the null hypothesis when, in fact, it is false) and reduces the statistical power of a test (Ellis, 2010b). As a statistical compromise, and as a result of conflicting advice from the statisticians conferred with during the process of analysing results, Bonferroni corrections were made in Paper II, but not in Paper III. Results should be interpreted in terms of both risks and advantages of the presence, or lack of corrections being made.

#### *Analysis of Covariance (ANCOVA)*

One-way analyses of covariance (ANCOVA) were used to control for possible effects of confounding variables (covariates) in observed changes post CRT. In Paper II, significant changes were observed in depression symptoms and BMI percentiles, and on a number of neuropsychological measures. In order to rule out potential effects of depression and weight changes on neuropsychological results at T2, the effect of baseline neuropsychological measures, the two covariates depression and weight, and an additional covariate labelled duration of illness (DOI), were controlled for using a univariate ANCOVA. Similarly, in paper III, univariate ANCOVA was used to explore changes in executive functioning between baseline and post-CRT, with baseline BRIEF scores and weight and depression as covariates (i.e. the two measures that changed significantly during the intervention). Preliminary checks were conducted to ensure that there was no violation of the assumption of normality and linearity, and that that correlations between covariates did not exceed  $r = .8$ .

## SUMMARY OF PAPERS AND UNPUBLISHED RESULTS

In this section, a short summary of each of the three papers is presented. All papers were published in peer-reviewed journals during 2013, and are presented directly after the list of references. In Appendix III, results from the CRT Treatment Evaluation Questionnaire are presented. Data from this questionnaire are currently unpublished, but included in the thesis as a measure of user feasibility.

### **Paper I - Developing and Evaluating Cognitive Remediation Therapy (CRT) for Adolescents with Anorexia Nervosa: A Feasibility Study**

*Objective:* CRT aims at improving neuropsychological weaknesses and associated thinking styles in patients with AN. It has only recently been developed for adolescents with AN, and evidence of its applicability for this particular patient group is limited. This study aimed to test the feasibility of individually tailored and delivered CRT for young females with AN.

*Methods:* A sample of 20 in- and outpatients (13-18 years) with AN participated in once- or twice weekly individual CRT sessions. The CRT materials used were available in a “CRT Resource Pack”. Feasibility was assessed with regards to the recruitment process, the delivery of the intervention, the materials used and clinical experiences.

*Results:* Overall results indicate that the intervention was feasible with regards to i) the recruitment of both in- and outpatients, ii) individual tailoring and delivery, iii) the CRT materials adapted to suit young females with AN, and iv) the acceptability for clinicians involved in the study. There were no voluntary dropouts with 19 of 20 patients completing the entire course of treatment.

*Conclusion:* The findings have implications for the refinement of CRT for the youngest AN population, and strengthens our understanding of the core components in the development and evaluation of novel interventions targeting AN. This study will help inform the design of a subsequent randomized controlled trial.

### **Paper II - Neuropsychological Functioning in Adolescents with Anorexia Nervosa Before and After Cognitive Remediation Therapy (CRT)**

*Objective:* To investigate neuropsychological functioning in adolescents with AN before and after receiving CRT.

*Method:* 20 young females with AN participated in an individually-delivered CRT treatment program. Neuropsychological and psychiatric assessments were administered before and after treatment. Weight, depression, anxiety, duration of illness and level of eating disorder psychopathology were considered as covariates in statistical analyses.

*Results:* Significant changes in weight, depression, visio-spatial memory, global information processing and verbal fluency were observed. Changes in weight had a significant effect on improvements in visuo-spatial memory and verbal fluency. Results also revealed a significant effect of depressive symptoms on perceptual disembedding abilities.

*Conclusion:* The results suggest improvements on a number of neuropsychological functions during the course of CRT. Future studies should explore the use of additional assessment instruments, and include control groups to assess the effectiveness of the intervention.

### **Paper III - Patient and Parental Self-Reports of Executive Functioning in a Sample of Young Female Adolescents with Anorexia Nervosa Before and After Cognitive Remediation Therapy**

*Objective:* Previous studies assessing the potency of CRT have largely focused on performance-based assessments, and how these change during the course of the intervention. Little is known of behavioural manifestations of such changes, and no previous studies have studied parental reports before and after CRT.

*Method:* Patient and parental self-reports of executive function using the BRIEF were obtained for 17 adolescent patients in treatment for AN before and after CRT.

*Results:* Results indicated that patients scored significantly lower on the BRIEF shift subscale post CRT, whereas parental reports revealed significantly lower scores on the shift and emotional control subscales, and on the two composite indices BRI and GEC. Case-wise comparisons support variations in executive functions in adolescents with AN.

*Conclusion:* Changes are evaluated in light of the relationship between patients and parents, and with regards to the limitations of the study design.

### **Unpublished Results – The CRT Treatment Evaluation Questionnaire**

18 out of 20 patients completed the treatment evaluation questionnaire post-CRT. The CRT Treatment Evaluation Questionnaire is presented in its entirety in Appendix II. Results from the questionnaire are based on CRT-specific items, but as response options differed

qualitatively between items, it was not possible to perform statistical analyses on this data material. Results are therefore presented using bar charts (see Appendix III). Item 12, 13, 14 and 15 are omitted, as these do not reflect changes associated with CRT per se. In summary, it appears as though the patients were satisfied with the course of CRT they had received, that pre-treatment information was sufficient, and that the sessions were both relevant and useful to the patients. Also, most patients reported having acquired skills that could be useful in their every-day life. The length of the sessions appeared to have been just right for most patients, although the majority would have wanted additional sessions. Most patients reported having become more aware of their own thinking processes as a result of CRT, but the intervention did not appear to have influenced the patients' ability to change in terms of their eating disorder, nor in relation to school or leisure and/or social activities. As for the relationship to the therapist, patients responded very positively with regards to all therapist-specific items.

## DISCUSSION

The main objective of this doctoral thesis was to assess the feasibility of CRT for young females with AN. By adopting the sequential approach to testing complex interventions put forth by the Medical Research Council (MRC) (Craig, et al., 2008), we achieved our aim of systematically evaluating the various components of the feasibility/piloting phase. We were able to conclude CRT is indeed feasible in terms of recruitment and retention, as well as with regards to the various procedures tested. Through this process, not only were we able to support the feasibility of CRT for young females with AN, but we simultaneously realized a number of those predictions described in the report by Baldock and Tchanturia (2007) (e.g. improvement of intervention designs, tailored CRT based on clinical profiles and delivery in both in- and outpatient settings). As the aim of the MRC feasibility/piloting trial is to produce a well-theorised, replicable intervention protocol (Mackenzie, 2010), our final objective was to either endorse embarking on a full-scale intervention, or suggest revisiting the original design in order to refine it before moving on to the subsequent phase in the MRC framework evaluation. The discourse that follows will try to shed light on the future of CRT, and will be based on the research objectives: patient recruitment and retention, treatment delivery and assessment methods and materials.

### **Patient Recruitment and Retention – Feasible but Generalizable?**

To our knowledge, the actual process of recruiting patients to CRT studies has not been addressed previously, and whereas former reports of CRT for AN have provided detailed information of included samples, little attention has been paid to the selection of participants, or factors associated with their consent or unwillingness to participate. The three papers included in this thesis are thus the first to address the process of recruiting patients to a CRT study and also the first systematically to evaluate the process and subsequently, classify it as *feasible*.

In general, it appears as though patients are willing to participate in CRT studies, and the treatment is commonly described as useful and stimulating by patients (Pitt, et al., 2010; Pretorius, et al., 2012; Whitney, et al., 2008). One possible contributor to the successful recruitment of patients to CRT studies might be the nature of the intervention, and its content. As far as our study is concerned, it was made a priority to emphasise CRT being a supplement

to ordinary treatment rather than replacing existing treatment engagements. The differences between CRT and traditional AN treatments were accentuated, and CRT-specific features such as the focus on the process of thought (the *how* of thinking) rather than the content of thinking (the *what*), the lack of focus on ED symptomatology, often emotionally charged, (such as weight, shape and/or food), might have rendered patients curious, rather than reluctant, and motivated rather than discouraged. As the standard is to offer CRT as a conjunctive therapy, and the nature of the intervention is fairly similar with regards to its content across studies, it is possible that the recruitment of patients to CRT in general is influenced by the nature of the therapy, and its foci. Also, a pivotal aspect of the recruitment of patients to our study was to delineate potential contributions of CRT at an early stage (e.g. raised awareness of one's own thinking styles), and areas in which one would not expect change (e.g. weight, ED psychopathology, co-morbidity) were communicated to patients, parents and clinicians so as to avoid unrealistic expectations. It is possible that these two aspects (i.e. the CRT content and clarification of potential outcomes) are of considerable worth in engaging patients in CRT, and presumably generalizable to studies beyond those described in this thesis.

In general, dropout rates in studies of CRT for AN are low, varying from 0 to 6 participants. However, although appealing to the eye, such numbers should be interpreted in terms of the size of the sample, and on the basis on number of sessions offered. A dropout rate of zero in single case studies (e.g. in Davies & Tchanturia, 2005, Pretorius & Tchanturia, 2007 and Tchanturia, et al., 2006) should not be confused with a dropout rate of zero in a larger sample, such as in the studies by Abbate-Daga, et al. (2012) and Dahlgren, et al. (2013b). In fact, when converting the number of participants who dropout from CRT to percentages, dropout rates vary from 0 to 25%. Compared to ordinary treatment for AN, these are lower rates in that it is not at all uncommon for drop out rates to exceed 30% (DeJong, Broadbent, & Schmidt, 2012; Hubert, et al., 2013). However, it is plausible that the low drop out rates in CRT studies in general represent the low number of sessions offered (ranging from 1-12), and that such rates would have increased considerably had the course of the intervention been extended in terms of number of sessions. Disregarding samples below 10 participants, the highest dropout rates (17 and 14% respectively) are found in CRT studies where the intervention has been delivered in groups (Genders & Tchanturia, 2010; Pretorius, et al., 2012). The lowest dropout rates (0 and 0% respectively), on the other hand, are found in

studies where CRT has been delivered individually (Abbate-Daga, et al., 2012; Dahlgren, et al., 2013a).

With regards to treatment retention, one might hypothesise that higher rates observed in individually delivered CRT are, in part, due to the treatment content, and the relationship to the CRT therapist. In individually delivered CRT, task assigned and discussions prompted are more specific to each patient's specific need, and hence, more relevant than when administered in a group setting. Although some of the advantages of delivering CRT in groups are that they are cost- and time efficient, and allows patients to share valuable experiences (Pitt, et al., 2010), one also risks targeting general weaknesses in cognitions and behaviors, rather than weaknesses specific to each patient. This hypothesis is partly supported by feedback from patients participating in group CRT, where sessions and assignments have been described as dull or repetitive, and group discussions problematic (Pretorius, et al., 2012). Also, fine-tuning the level of task difficulty in groups has been reported being challenging, and unfavourable group dynamics have been described (Wood, et al., 2011; Zuchova, et al., 2013). Another advantage of individually delivered and tailored CRT sessions might be that they strengthen the bond between the therapist and the patient. A good therapeutic alliance is known to predict treatment adherence and better outcomes, and it is not unlikely that the relationship between a CRT therapist and her/his patient is characterized by a stronger sense of common goals, trust and safety in those working on a one-to-one basis with their therapist, than those receiving CRT in groups. However, at this point, these are mere speculations warranting further investigation.

Acceptance to engage in CRT, and low dropout are evidence of feasibility. However, are the results obtained in our study generalizable, i.e. can researchers replicate our recruitment processes, and expect similar results? Firstly, it is important to point out that our sample was a convenience sample rather than a sample based on a predetermined set of characteristics (if we disregard the inclusion criteria). This implies a heterogeneous sample varying in, for example, age, developmental status, personality, and levels of psychiatric comorbidity. The sample also reflects heterogeneity as it consists of both in- and outpatients. Although these aspects lead to greater individual differences, they simultaneously strengthen the possibility of generalizing findings in terms of recruitment and retention. Despite the fact that the sample was heterogeneous, we did not experience any discrepancies in terms of who (in- or outpatient) accepted the invitation to participate, or who remained in treatment. Thus, it is plausible for other researchers to adopt the same approach as we did to obtain similar results.

Finally, it is important to note that there might be a causal relationship between the rate of retention and the mode of delivery in our study. To state it more clearly, it is likely that altering the delivery structure to suit the individual need of each patient might have had an effect on the rate of retention. Had we been more stringent in terms of the intensity of sessions, and less flexible with regards to accommodating the patients based on their availability, it is highly likely that we would have experienced an elevated dropout rate. As the participants in our study were part of a research project, patients were accommodated (i.e. with regards to rescheduling sessions) to an extent that would perhaps not have been possible had the intervention been given in a clinical setting, delivered by people with a time schedule allowing less flexibility. The flexibility of the therapist does thus appear to play an important role in treatment retention.

### **Treatment Delivery – Feasible but Replicable?**

CRT for patients with AN was originally delivered individually, and this mode of delivery was adhered to during at least five years after the first case study was published. In 2010, the first study reporting the acceptability of group CRT was published (Genders & Tchanturia, 2010) and in 2013, the mode of delivery was even further developed when Lask & Roberts (2013) presented the first report of family CRT, followed by Brockmeyer et al's (2013) additive study investigating the combination of individually delivered, and computer assisted CRT sessions. As evident from the literature review presented in this thesis, the mode in which CRT is being delivered is changing rapidly, and as new modalities are described, tested and evaluated, it is crucial to attempt comparing results so as to understand the advantages and disadvantages of each approach.

Whereas individual CRT appears to be associated with lower dropout rates and the potential of creating a positive patient- therapist alliance, disadvantages with this mode of delivery concerns the lack of efficiency in terms of time and resources used. Group therapy appears to appeal to patients in increasing awareness of shared cognitive styles, but has also been reported fostering negative group dynamics, and tasks assigned during the therapy is not always perceived as relevant. At present, there is only one report of family CRT (Lask & Roberts, 2013), and although it appears as family CRT strengthens the understanding of how cognitive styles affect family dynamics, improves communication and cooperation during

treatment, one must stress that family CRT should not replace existing treatments, but rather be seen as a adjunct to ordinary treatment engagements. Also, it might be worth considering the complexity of interfamily processes that take place during CRT, and be careful not to bring in issues that are not directly related to CRT, but belong in other discussion forums.

Attempting to evaluate previous finding in terms of delivery, it is clear that the majority of studies have used materials from the manual developed for CRT with adults (Tchanturia & Davies, 2010). However, these materials have never been published, nor systematically evaluated. Also, it appears as though there are large variations in how these materials have been applied in treatment. As a result of large discrepancies between materials applied, poor descriptions and a consistent lack of systematic evaluation, it is difficult to know if patients have received the same type of treatment, and what (if any) aspects of treatment are commonly shared. As a consequence, it is difficult to establish treatment fidelity, or the lack of it. The aspect of fidelity to treatment is closely related not only to *what types* of materials are being used to deliver CRT, but also *how* these are applied during treatment. At present, there are no general guidelines for how to deliver CRT, and it appears as though many of those delivering the intervention have not attended any type of formal training. The question of who can, or who should, deliver CRT is definitely an issue that requires more attention, and will guide both future research studies and clinical implementation.

As the goal of this feasibility trial was to investigate the possibility of producing a replicable (and useful) protocol, we must also scrutinize our own approach in delivering CRT, and the extent to which we can support our own treatment fidelity. Although the materials we used were evaluated continuously and labelled feasible, we were not able to record any of the sessions on video. We did, however, record all sessions in the electronic hospital registry which shows that the same materials have been used with all patients, and the focus of the sessions have, almost exclusively, been a combination of practical tasks and reflections on thinking styles. However, as we have tailored the sessions to suit each patient's individual needs, developmental status and cognitive style, tasks have varied (but always within the scope of tasks presented in Appendix I), and so have homework exercises. It might therefore be more valuable for researchers aiming to replicate our study design to adopt an approach combining fidelity and flexibility, as the ultimate goal of the intervention is to help each individual patient, rather than adhering rigidly to a fixed design.

## **Assessment Methods and Materials – Feasible but Useful?**

As previously pointed out, CRT research has largely focused on using neuropsychological performance based tests to assess changes associated with CRT, and adults studies are in the majority. The three papers presented in this thesis, however, were pioneering in investigating the feasibility of CRT for adolescents with AN, and at the initiation of this project, little was known about the neurocognitive profile of young females with AN. As a result of clinical observations suggesting weaknesses in neurocognitive functioning in young patients with AN (i.e. rigidity and excessive detail focus), outcome measures similar to those used in adult samples were chosen to investigate post CRT functioning in our sample. As the project progressed, however, literature started emerging suggesting the neurocognitive profile of young AN patients being less distinct than that of adults. On a group level, our results supported several previous findings failing to find neuropsychological weaknesses in adolescents with AN (Bühren, et al., 2012; Fitzpatrick, et al., 2012; Rose, et al., 2012; Rose, Stedal, Watkins, Frampton, & Lask, In Press; Shott, et al., 2012), but on an individual level, heterogeneous results emerged supporting the possibility of potential sub-group phenomena (Rose, et al., 2012; Rose, et al., In Press), or at the least, the lack of homogeneity.

Several hypotheses have been put forward to explain why the neurocognitive profiles of young AN patients differ from those of adults. According to Roberts et al. (2012), poor set-shifting is a AN sub-group phenomena with AN-BP patients scoring significantly poorer than AN-R patients. Due to the small size of our sample (N=20) and the lack of information regarding AN-BP or AN-R diagnostic categorizing, we were not able to explore such group differences. Another perspective is put forth by Bühren et al. (2012) who argue that set-shifting in children and adolescents is a skill that has yet to evolve, and that the brain maturation, especially the cortico-striatal networks that modulate set-shifting, are not fully developed until early thirties, and thus, can not be labelled defective. Based on this hypothesis, one would expect variations in cognitive functioning, and specific deficits would be difficult to detect due to variations in the developmental trajectory.

Further, whereas most studies exploring neuropsychological performance in AN patients have supported both weak set-shifting and poor central coherence, it is important to note that these are adults studies, and that the samples they represent might be a subgroup of all those who develop the disorder. Since the peak onset of AN is during adolescence, one must take into

consideration that a significant percentage of those afflicted recover before entering adulthood and hence, are never included in adult studies. One possibility is therefore that young AN individuals displaying normal cognitive functioning are simply not neuropsychologically weakened, and belong to the group that recovers from the illness before entering adulthood.

The state or trait debate can also be useful in explaining differences in neuropsychological functioning in AN. Several previous studies have suggested weaknesses in neuropsychological functioning being consequences of the illness, and representing a scarring effect with its severity depending of the duration of illness (Danner, et al., 2012; Harrison, Tchanturia, & Treasure, 2011; Hatch, et al., 2010). In line with this hypothesis, it is possible that, although many young patients with AN do not exhibit neuropsychological weaknesses, such will emerge as the illness progress, and hence, be detectable as the course of the illness extends.

It is also possible that instruments used to assess neuropsychological functioning are not sensitive enough to capture weaknesses as they appear in contextually meaningful settings. Clinically, many young patients with AN are undoubtedly struggling with both flexibility and global information processing, especially in terms of ED specific symptoms such as preoccupations with weight, food, calories, shape, and purging behaviors. However, as these weaknesses do not always appear to manifest in a controlled test-setting, this might indicate low sensitivity of assessment measures (e.g. the test in the Ravello Profile), that is, that they are not sensitive enough to pick up on modest neuropsychological weaknesses, or perhaps even more realistic, that rigidity and detail focus related to everyday life activities are non-assessable using neuropsychological test, i.e., that these lack ecological invalidity.

As illustrated above, a number of plausible explanations can help explain the discrepancy between adolescent and adult neurocognitive profiles. However, hypotheses used to explain such discrepancies are purely speculative, warranting studies of alternative designs, and especially, longitudinal studies to illuminate the cause of such differences. One should, however, bear in mind that neuropsychological studies in young females with AN are far fewer, and sample sizes smaller than in adult studies. The sizes of these samples will undoubtedly have an impact on the significance of results, and the generalizability of these. Also, there is emerging evidence of neuropsychological functioning subtypes in AN (Rose, et al., In Press), rendering it possible for undetected sub group phenomena in small samples. It is

thus possible that there are, in fact, also young individuals with AN displaying weak neurocognitive functioning, but that group level analyses fail to recognise such individual differences.

There is no doubt that the assessment instruments used in the three studies presented in this thesis are feasible to distribute and/or administer, and as there is limited counterevidence, one would assume that so are assessments instruments used in previous CRT studies. However, there is a significant difference between that of being feasible, and that of being useful. Revisiting the CRT literature, there is only one previous study assessing post CRT changes in adolescents (Pretorius, et al., 2012). Similar to the results from the treatment evaluation questionnaire presented in Appendix II, adolescents in Pretorius et al.'s study reported CRT being helpful, and patients fed back that they liked that the intervention encouraged metacognition and behavioural changes. However, to investigate post CRT functioning, Pretorius et al. chose to focus on self-reported cognitive flexibility using the cognitive flexibility scale (CFS) (Martin & Rubin, 2005) and motivation to change, none of which were found to have changed significantly during the course of the intervention. Also, although pre CRT CFS scores were lower compared to healthy controls (Martin & Rubin, 2005) it is possible that these scores are state related (i.e. due to malnutrition and/or underweight) rather than being stable traits. As the instruments used in Pretorius et al.'s study differ significantly from those used in our three studies, results are difficult to compare. Nevertheless, the methods of assessment used in Pretorius et al. (2012) might be indicative of how such instruments can (or could) make an important contribution to performance based test commonly applied in pre-post CRT assessments.

As we continue chasing statistically significant changes in groups that are already performing within norms, we inevitably risk neglecting changes that are too small to show up in any statistical test, but that are clinically meaningful in terms of the everyday life of our patients. Also, as we assume results from group analyses being representative for the AN population as a whole, we risk losing valuable information in terms of individual changes, and implications of treatment outcomes specific to each patient. The treatment evaluation questionnaire presented in Appendix II can be used to illustrate both these both points. Feedback from patients clearly indicates CRT being useful and relevant to the patients, and also suggests that patients have become more aware of their own thinking styles during the course of the intervention. Such results will be difficult to obtain through, for example,

performance-based testing such as the Ravello Profile, but do, perhaps, more accurately represent the true value of CRT. Rather than remedying a fault or a weakness, perhaps CRT for young patients with AN can be viewed as a neutral environment where skills necessary for change are learned, and where patients acquire knowledge of how to manage responses in an efficient way, and develop coping behaviors useful in everyday life activities.

The term “remediate” stems from the noun “remedy”, which according to the Oxford English Dictionary (Oxford English Dictionary, Accessed November 22, 2013) refers to “*A cure for a disease, disorder, injury, etc.; a medicine or treatment that promotes healing or alleviates symptoms*”. The literal meaning of the term “to remediate” is then the act or process of correcting a fault or deficiency (Wykes & Reeder, 2005). The concept of remediation is perhaps appropriate for use when treating adults who, according to the literature, actually display neurocognitive weaknesses. However, are we accurate in using the term remediate for younger patients with AN who display a far more complex variation of cognitive functioning, or are the active components when applied for this patient group different?

In conclusion, it is perhaps time for a shift of paradigms. As improving neuropsychological functioning might not be relevant to all patients with AN, it might be a good time to revisit one of the original aims of the intervention; preparation for subsequent treatment (Davies & Tchanturia, 2005; Pretorius & Tchanturia, 2007), but also to pay attention to results recently surfaced such as attrition reduction (Lock, et al., 2013). And as CRT aims to address thoughts and behaviors as they manifest in the patient’s everyday life, novel measures such as metacognitive abilities, quality of life or every day coping strategies might be useful in assessing outcomes associated with the intervention, rather than focusing on experimental measures with poor ecological validity.

### **Strengths and Limitations**

There are both strengths and limitations to existing CRT studies, including the three studies presented in this doctoral thesis. Some of these have been previously attended to, and are described in Paper I-III. Others have received less attention, and will be delineated in this section.

On an overall basis, there are numerous strengths to previous CRT studies. Firstly, they represent a range of delivery modes, all of which appear to be feasible and acceptable to patients. Secondly, CRT appears to suit patients from all age groups, regardless of illness severity and other treatment engagements. Thirdly, the great variety of assessment methods and materials used can help demonstrate the range of outcomes one can expect be associated with CRT. However, despite the fact that there has been a considerable growth in publications investigating CRT for AN during the last decade, a continued limitation in the field is the still small number of studies assessing the effect of the therapy, and the discrepancies in the hypothesized potency of the intervention. Of the 21 studies included in the literature review, 19 studies included functional outcome measures varying widely in terms of whether they were rated by a clinician, performance-based or self-reports, from patients and/or parents, and only 2 studies reported data from RCT's. It seems highly unlikely that interventions would produce equivalent effects on such a variety of outcome measures, and that one would, on the basis of existing studies, be able to generalize findings. Also, as the development and evaluation of CRT for adolescents with AN is still in an early phase, and findings from neuropsychological studies do not provide consistent findings in neurocognitive functioning, one might be tempted to question whether CRT actually remediates cognitive weaknesses in this patient group, or if there are other factors contributing to observed changes, and positive patient feedback.

As for strengths more specific to the three studies included in this thesis, the first concerns the fact that these studies are pioneering in testing the feasibility of CRT developed specifically for *adolescents* with AN. They are also the first studies applying a well-documented framework (the MRC framework) to systematically evaluate the various components of this feasibility/piloting trial. Further, parental and patients reports of executive functions have not previously been assessed before and after CRT, and together, the results presented in Paper I-III strengthen previous research evidence suggesting heterogeneity in neuropsychological functioning in young individuals with AN. However, there are also some limitations to note. Firstly, as participants represent patients from two specialist units, it is difficult to know how less severely ill patients would have responded to CRT. Also, as the sample was recruited with the aim of conducting a research study, it is possible that the group was biased in terms of treatment motivation, that is, that participants were more motivated to engage in treatment since they could choose to accept or decline the invitation to participate. It is thus possible that the patients included in this project had a more favourable outcome in terms of treatment

satisfaction and adherence, than if they had they been given no choice in whether to participate or not.

Further, it is worth noting that, similar to previous studies assessing pre and post CRT functioning using performance based test, learning effects undoubtedly biased results. It is not unreasonable to assume that although statistical analyses were controlled for multiple comparisons, learning effects were present, and perhaps especially prone to compromise results where an element of surprise, such as in the recall condition of the RCFT, was present. Also, as far as assessment methods are concerned, norms from adult samples were used to evaluate results from the Brixton test, and the CCI, SI and OCI from the RCFT. It is therefore plausible that results obtained from these measures are skewed, and that we would have obtained different results had we used age appropriate norms. On the other hand, even though adult norms were used for our patient sample, patients performed within the normal range, indicating that one could have expected elevated levels had one used age corrected norm data to compare results.

Yet another weakness concerns the process of delivery. Altogether, the participants appeared to find CRT useful and relevant, and the vast majority of participants reported being very satisfied with the relationship to the CRT therapist. However, since it is well documented that a good alliance between the patient and the therapist is central to engaging patients and motivating them to stay in treatment, it is possible that the role of the therapist played an important part in treatment adherence. In our study, only one therapist delivered CRT, and it is therefore not possible to exclude a therapist-specific contribution to the low dropout. If these results can be reproduced in other contexts where several therapists deliver CRT remains to be investigated. Also, as we lack the diagnostic information regarding AN subtypes (AN-R and AN-BP), we can not tell if differences between these groups in terms of neuropsychological functioning, comorbidity and ED psychopathology have had an impact on pre and post CRT assessments, treatment retention and satisfaction.

The final remark relevant to the weaknesses of our own research study is also related to the challenges of interpreting results. Although several changes were significant post CRT, we cannot interpret these as being direct results of the intervention itself. All patients received CRT as a adjunct to treatment as usual, and the specific contribution of CRT cannot be separated from other intervention effects, or external factors. However, as assessing the effect

of CRT was not the primary aim of these studies, this issue should perhaps not be listed as a limitation, but rather as an issue warranting further investigation in future research studies.

### **Future Research Implications**

To enhance our understanding of mechanisms of action in CRT, future studies should clearly outline the aim(s) of delivering CRT to patients with AN, using study designs appropriate for testing hypotheses of specific intervention outcomes. Considering the emergence of heterogeneity in neuropsychological functioning in young individuals with AN, novel outcome measures such as metacognitive abilities, self-awareness, motivation, ability and willingness to change and therapeutic alliance might make important contributions to the understanding of the effects of CRT. Also, as feasibility of CRT for AN has been established across ages, illness severity and cognitive functioning, it is perhaps time to shift focus from that of feasibility trials, to studies in which the effect of the intervention can be assessed. Further, results presented in Paper III might help guide the development and evaluation of CRT for families, which might serve as a useful addition to the fairly limited scope of treatments for young females with AN. Finally, as one of the essential steps of a feasibility trial is to produce a replicable protocol that can be used in subsequent RCT's, future studies should take advantage of the data presented in the three papers in this thesis to calculate the appropriate sample size necessary to detect changes associated with CRT.

## CONCLUSION

The aim of this thesis was to test the feasibility of cognitive remediation therapy for adolescents with AN. In light of the results presented in Paper I-III, findings suggest that the intervention is feasible for this patient group, and contributes to the field by i) supporting the implementation of CRT in a mixed sample, ii) supporting heterogeneity in neuropsychological functioning, iii) challenging the use of neuropsychological assessment instruments to assess changes associated with CRT in adolescents, iv) illustrating discrepancies between patient and parental ratings pre- and post-CRT, and v) encouraging novel approaches to test the potency of CRT for young patients with AN.

According to results presented in Paper I-III, and additional remarks presented in this thesis, revisiting and altering the design of the study is suggested before embarking on a full-scale intervention. Also, as there are inconsistencies in neuropsychological functioning in adolescents with AN, cognitive *remediation* therapy might not be a suitable intervention title for all patients with AN. As one crucial component of the intervention is to increase awareness of cognitive processes, the PhD candidate suggests re-labelling the intervention for the younger AN population to Metacognitive Enhancement Therapy for AN (META).

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## **PAPER I**

Dahlgren, C.L., Lask, B., Landrø, NI & Rø, Ø. (2013). Developing and Evaluating Cognitive Remediation Therapy for Adolescents with Anorexia Nervosa: A Feasibility Study. *Clinical Child Psychology and Psychiatry*. [Epub ahead of print]. DOI: 10.1177/1359104513489980



## PAPER II

Dahlgren, C.L., Lask, B., Landrø, NI & Rø, Ø. (2013). Neuropsychological Functioning in Adolescents with Anorexia Nervosa Before and After Cognitive Remediation Therapy: A Feasibility Trial. *International Journal of Eating Disorders*. 46(6):576-81. DOI: 10.1002/eat.22155.



### **PAPER III**

Dahlgren, C.L., Lask, B., Landrø, NI & Rø, Ø. (2013). Patient and Parental Self-Reports of Executive Functioning in a Sample of Young Females with Anorexia Nervosa Before and After Cognitive Remediation Therapy. *European Eating Disorders Review*. [Epub ahead of print]. DOI: 10.1002/erv.2265.

